Semi-Automating Knowledge Base Construction for Cancer Genetics

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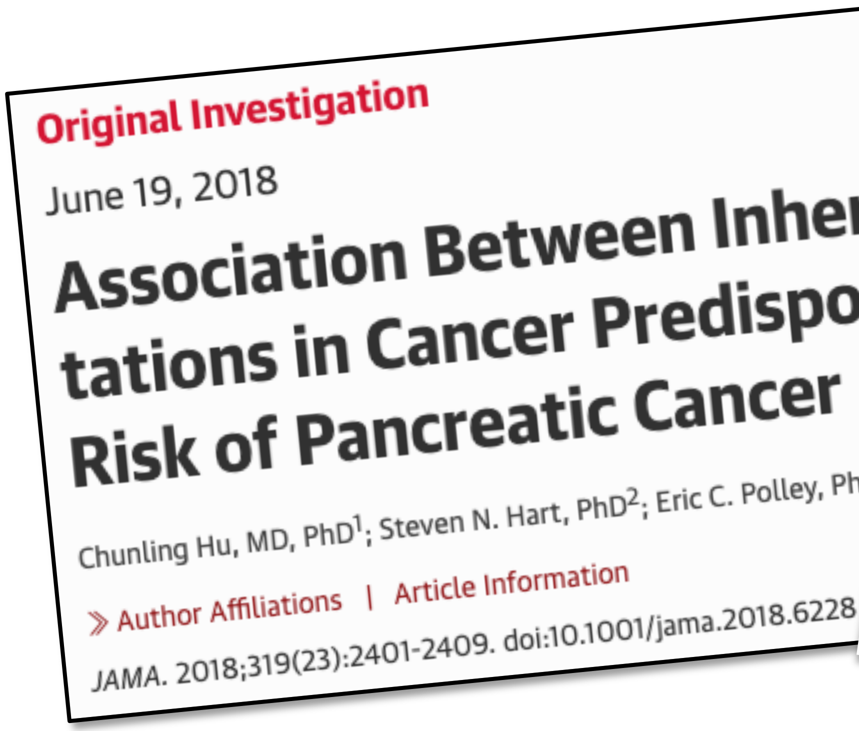
HARVARD MEDICAL SCHOOL

Appraising oncology literature

Penetrance papers Medical literature describing risk of cancer with a particular pathogenic variant in cancer susceptibility gene.



Original Investigation

June 19, 2018

Association Between Inherit tations in Cancer Predisposi Risk of Pancreatic Cancer

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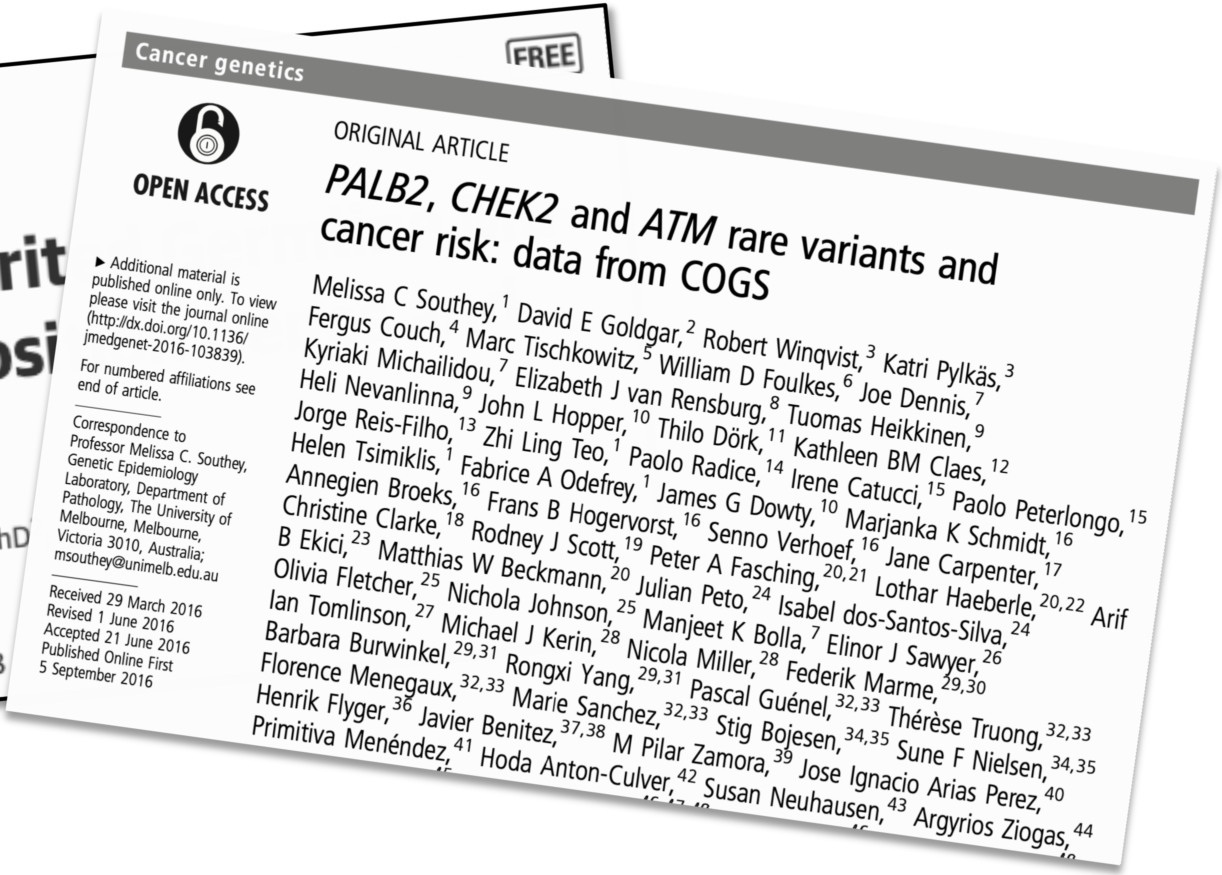
» Author Affiliations | Article Information

JAMA. 2018;319(23):2401-2409. doi:10.1001/jama.2018.6228



Cancer genetics FREE

OPEN ACCESS

ORIGINAL ARTICLE

PALB2, *CHEK2* and *ATM* rare variants and cancer risk: data from COGS

Melissa C Southey,[1] David E Goldgar,[2] Robert Winqvist,[3] Katri Pylkäs,[3] Fergus Couch,[4] Marc Tischkowitz,[5] William D Foulkes,[6] Joe Dennis,[7] Kyriaki Michailidou,[7] Elizabeth J van Rensburg,[8] Tuomas Heikkinen,[9] Heli Nevanlinna,[9] John L Hopper,[10] Thilo Dörk,[11] Kathleen BM Claes,[12] Jorge Reis-Filho,[13] Zhi Ling Teo,[1] Paolo Radice,[14] Irene Catucci,[15] Paolo Peterlongo,[15] Helen Tsimiklis,[1] Fabrice A Odefrey,[1] James G Dowty,[10] Marjanka K Schmidt,[16] Annegien Broeks,[16] Frans B Hogervorst,[16] Senno Verhoef,[16] Jane Carpenter,[17] Christine Clarke,[18] Rodney J Scott,[19] Peter A Fasching,[20,21] Lothar Haeberle,[20,22] Arif B Ekici,[23] Matthias W Beckmann,[20] Julian Peto,[24] Isabel dos-Santos-Silva,[24] Olivia Fletcher,[25] Nichola Johnson,[25] Manjeet K Bolla,[7] Elinor J Sawyer,[26] Ian Tomlinson,[27] Michael J Kerin,[28] Nicola Miller,[28] Federik Marme,[29,30] Barbara Burwinkel,[29,31] Rongxi Yang,[29,31] Pascal Guénel,[32,33] Thérèse Truong,[32,33] Florence Menegaux,[32,33] Marie Sanchez,[32,33] Stig Bojesen,[34,35] Sune F Nielsen,[34,35] Henrik Flyger,[36] Javier Benitez,[37,38] M Pilar Zamora,[39] Jose Ignacio Arias Perez,[40] Primitiva Menéndez,[41] Hoda Anton-Culver,[42] Susan Neuhausen,[43] Argyrios Ziogas,[44]

▸ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/jmedgenet-2016-103839).

For numbered affiliations see end of article.

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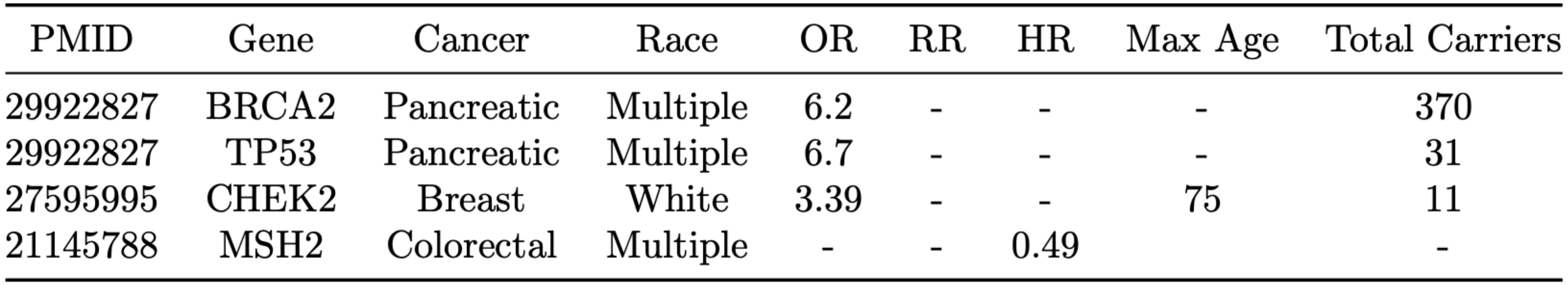
Key study information

- What population was studied? ***Ascertainment***!
- How many patients were in the study?
- What cancer was the patient at-risk for? What was the associated risk?
- Ideally: Synthesize the key elements from papers into a database.
    - e.g. ask2me.org



PMID	Gene	Cancer	Race	OR	RR	HR	Max Age	Total Carriers
29922827	BRCA2	Pancreatic	Multiple	6.2	-	-	-	370
29922827	TP53	Pancreatic	Multiple	6.7	-	-	-	31
27595995	CHEK2	Breast	White	3.39	-	-	75	11
21145788	MSH2	Colorectal	Multiple	-	-	0.49		-

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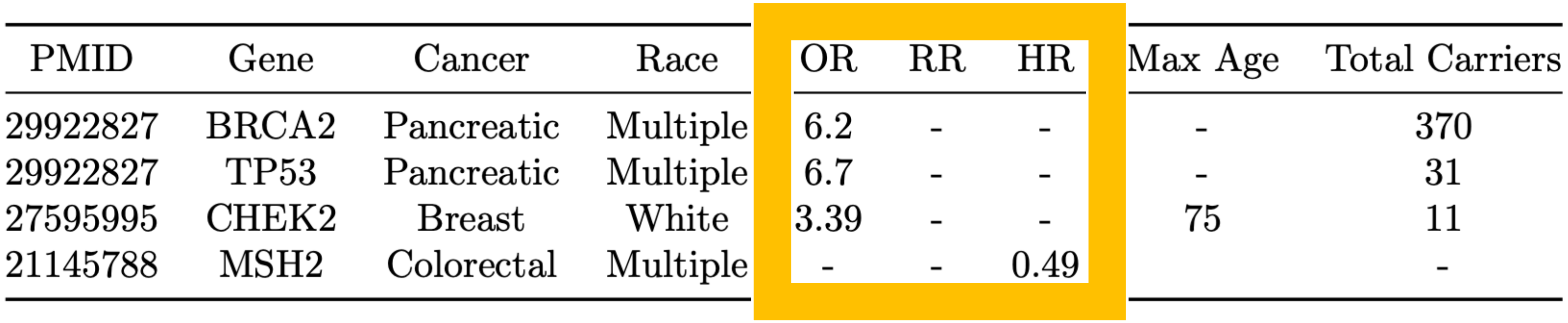

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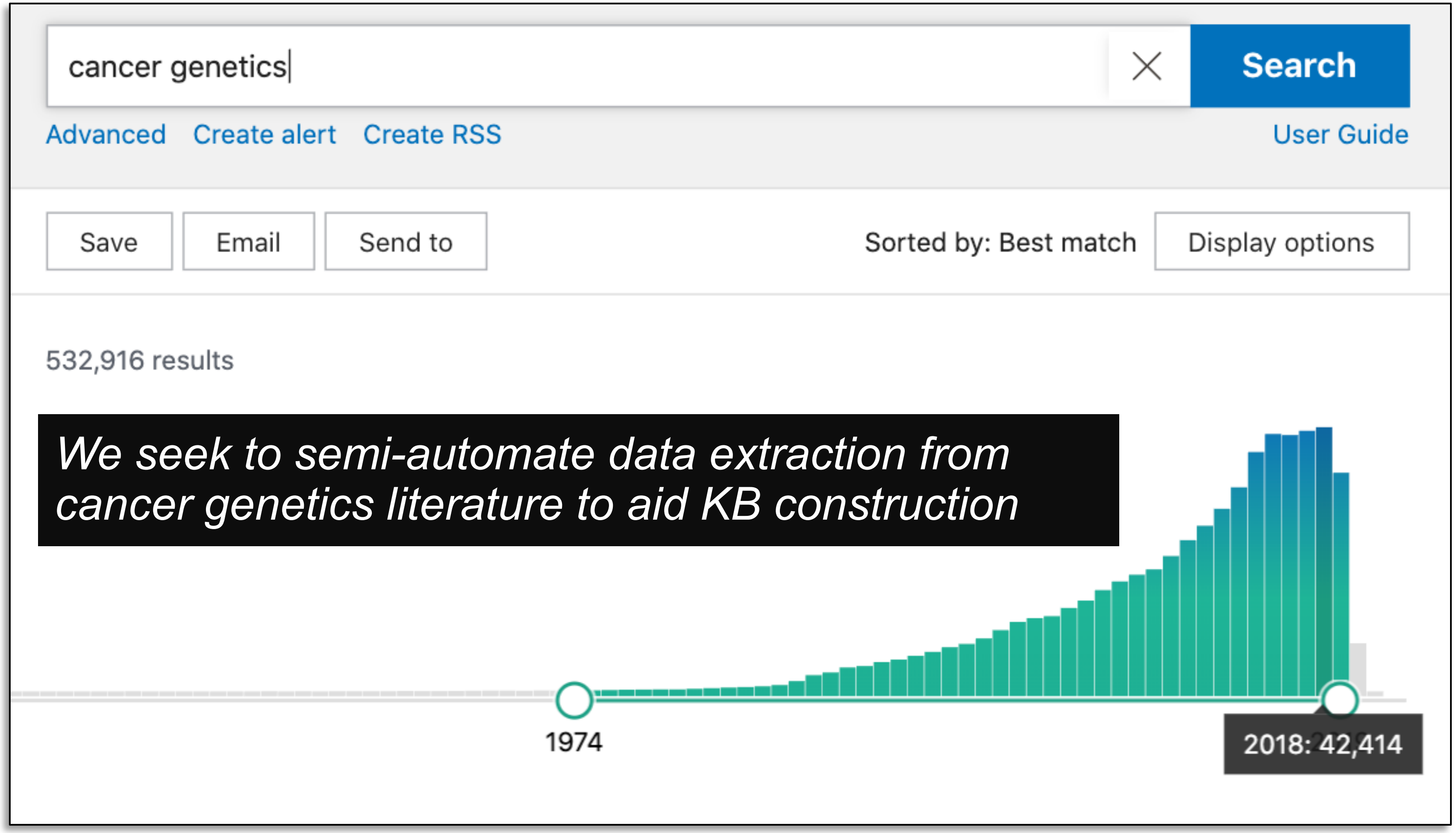
The problem: Too many studies



cancer genetics

532,916 results

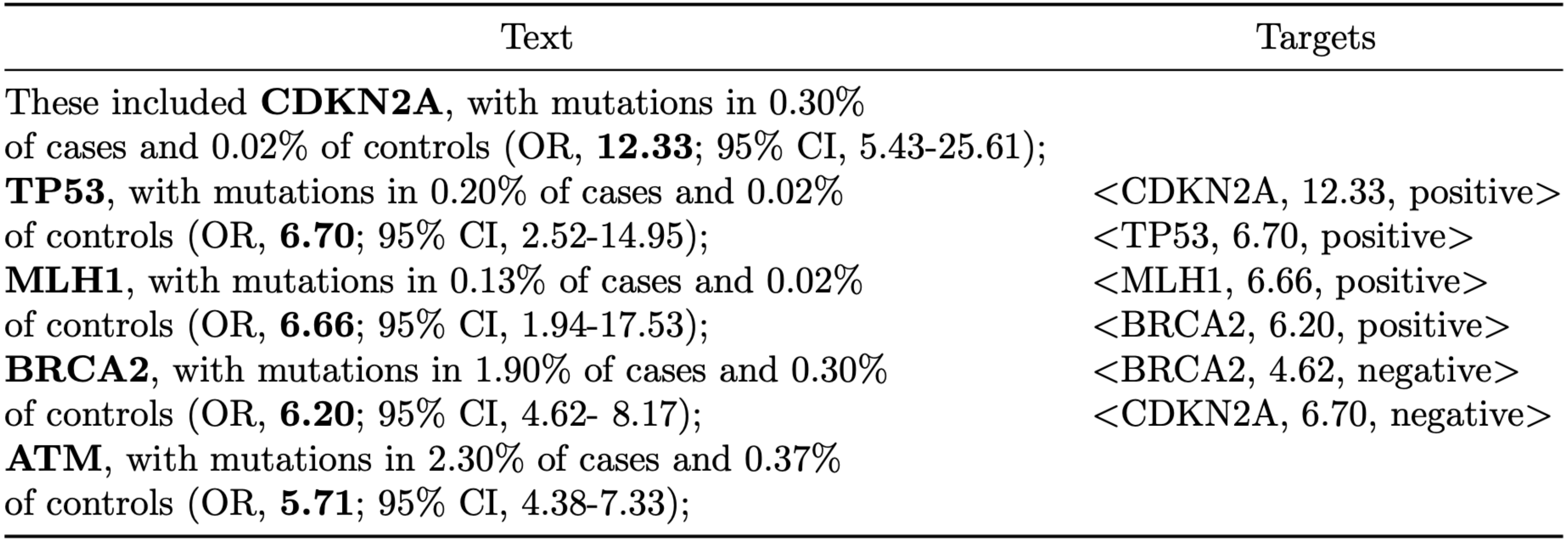
We seek to semi-automate data extraction from cancer genetics literature to aid KB construction

Ascertainment

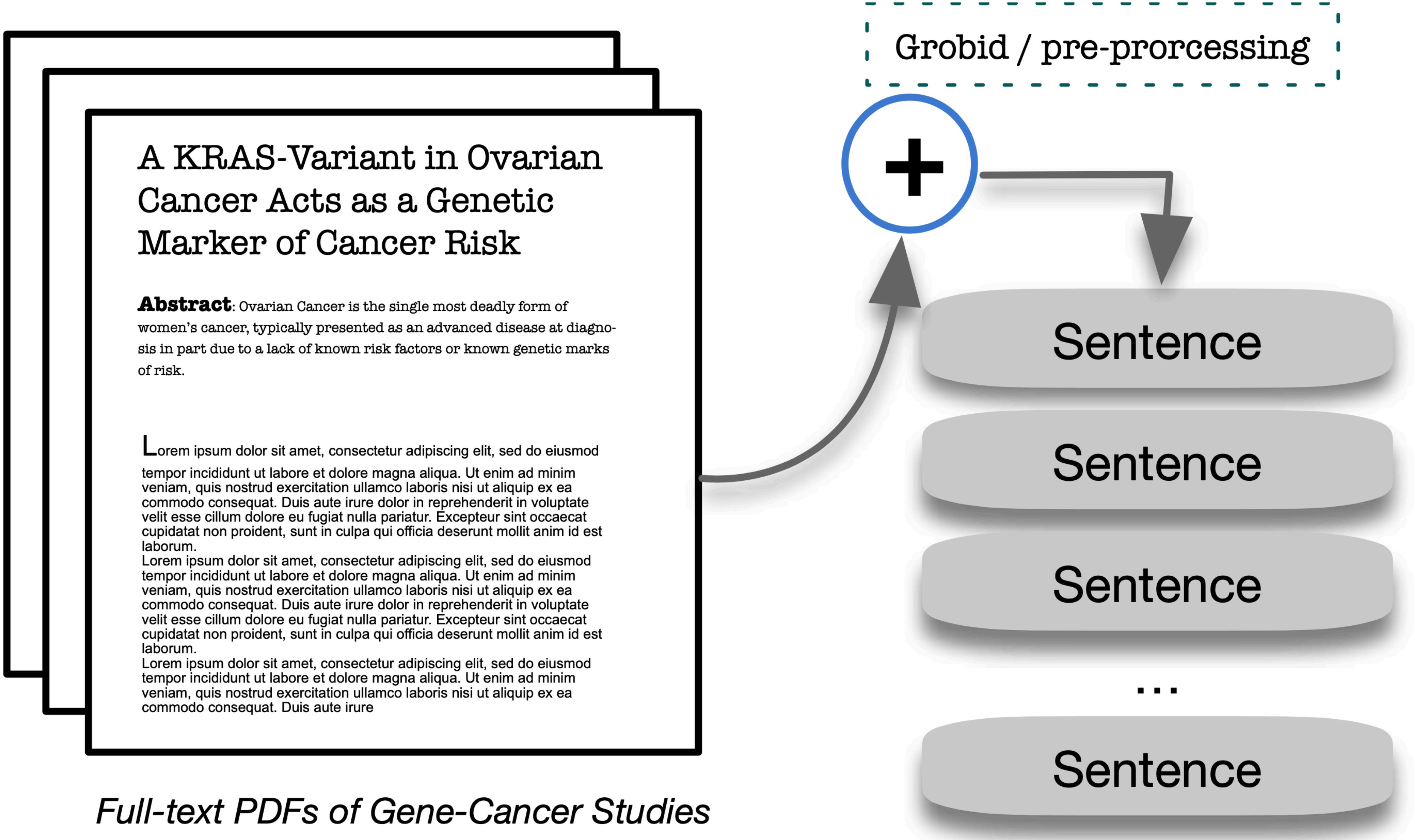
A control population was defined from the National Danish Civil Registration System, matched for sex, year of birth, mutation carriers as well as first degree relatives.

For age adjusted analysis, the projected U.S. population was used (year 2000); 84% of the 3499 individuals were white.

Risks



Text	Targets
These included **CDKN2A**, with mutations in 0.30% of cases and 0.02% of controls (OR, **12.33**; 95% CI, 5.43-25.61); **TP53**, with mutations in 0.20% of cases and 0.02% of controls (OR, **6.70**; 95% CI, 2.52-14.95); **MLH1**, with mutations in 0.13% of cases and 0.02% of controls (OR, **6.66**; 95% CI, 1.94-17.53); **BRCA2**, with mutations in 1.90% of cases and 0.30% of controls (OR, **6.20**; 95% CI, 4.62- 8.17); **ATM**, with mutations in 2.30% of cases and 0.37% of controls (OR, **5.71**; 95% CI, 4.38-7.33);	<CDKN2A, 12.33, positive> <TP53, 6.70, positive> <MLH1, 6.66, positive> <BRCA2, 6.20, positive> <BRCA2, 4.62, negative> <CDKN2A, 6.70, negative>



A KRAS-Variant in Ovarian Cancer Acts as a Genetic Marker of Cancer Risk

Abstract: Ovarian Cancer is the single most deadly form of women's cancer, typically presented as an advanced disease at diagnosis in part due to a lack of known risk factors or known genetic marks of risk.

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Sentence

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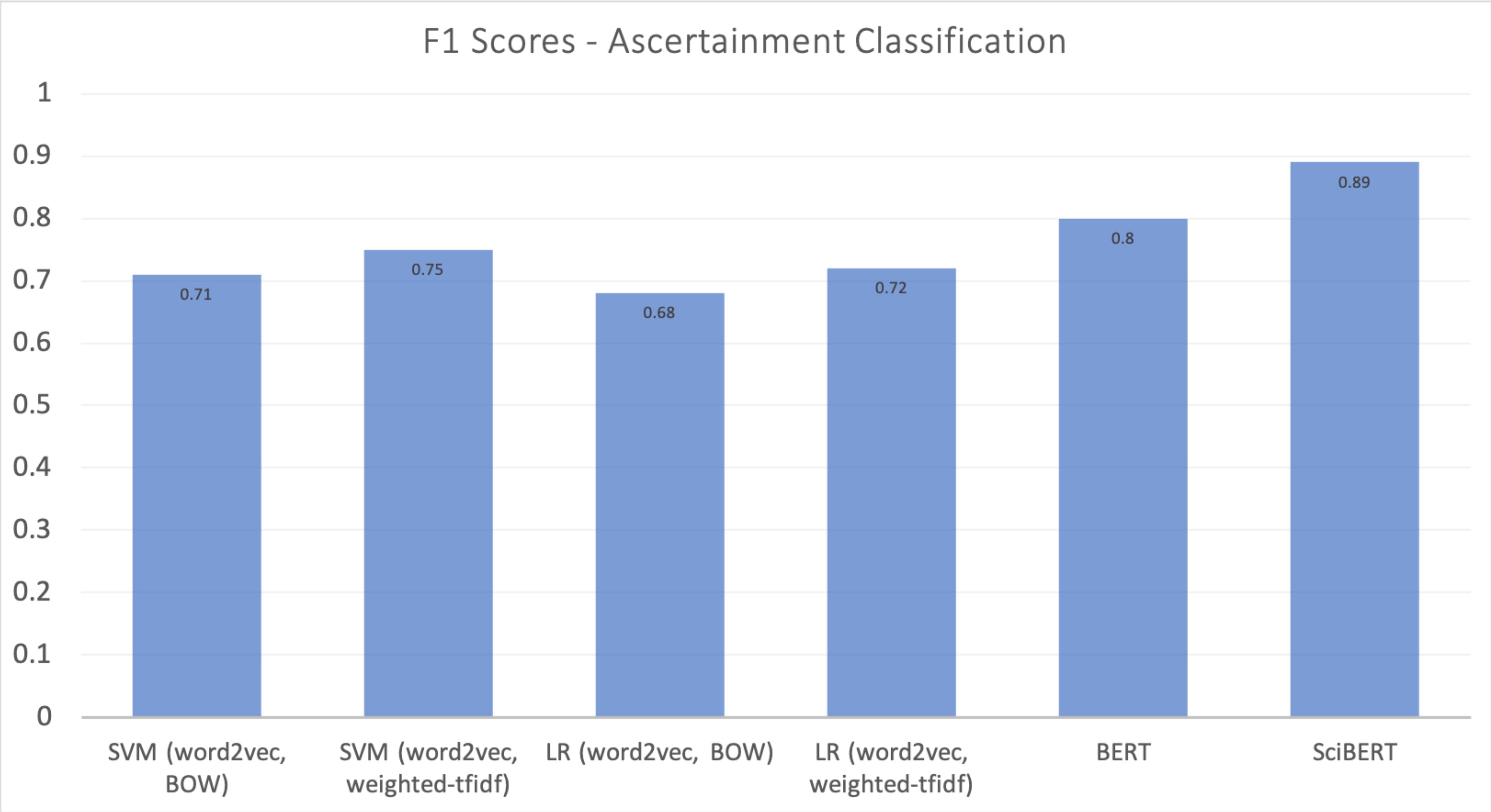
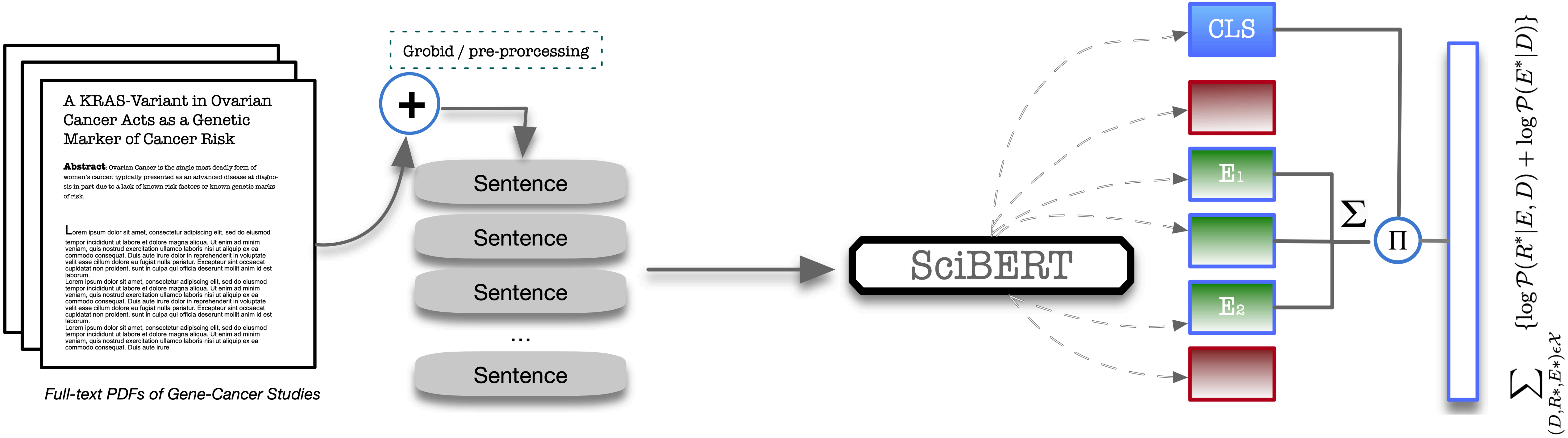
Full-text PDFs of Gene-Cancer Studies


F1 Scores - Ascertainment Classification
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.71
0.75
0.68
0.72
0.8
0.89
SVM (word2vec, BOW)
SVM (word2vec, weighted-tfidf)
LR (word2vec, BOW)
LR (word2vec, weighted-tfidf)
BERT
SciBERT



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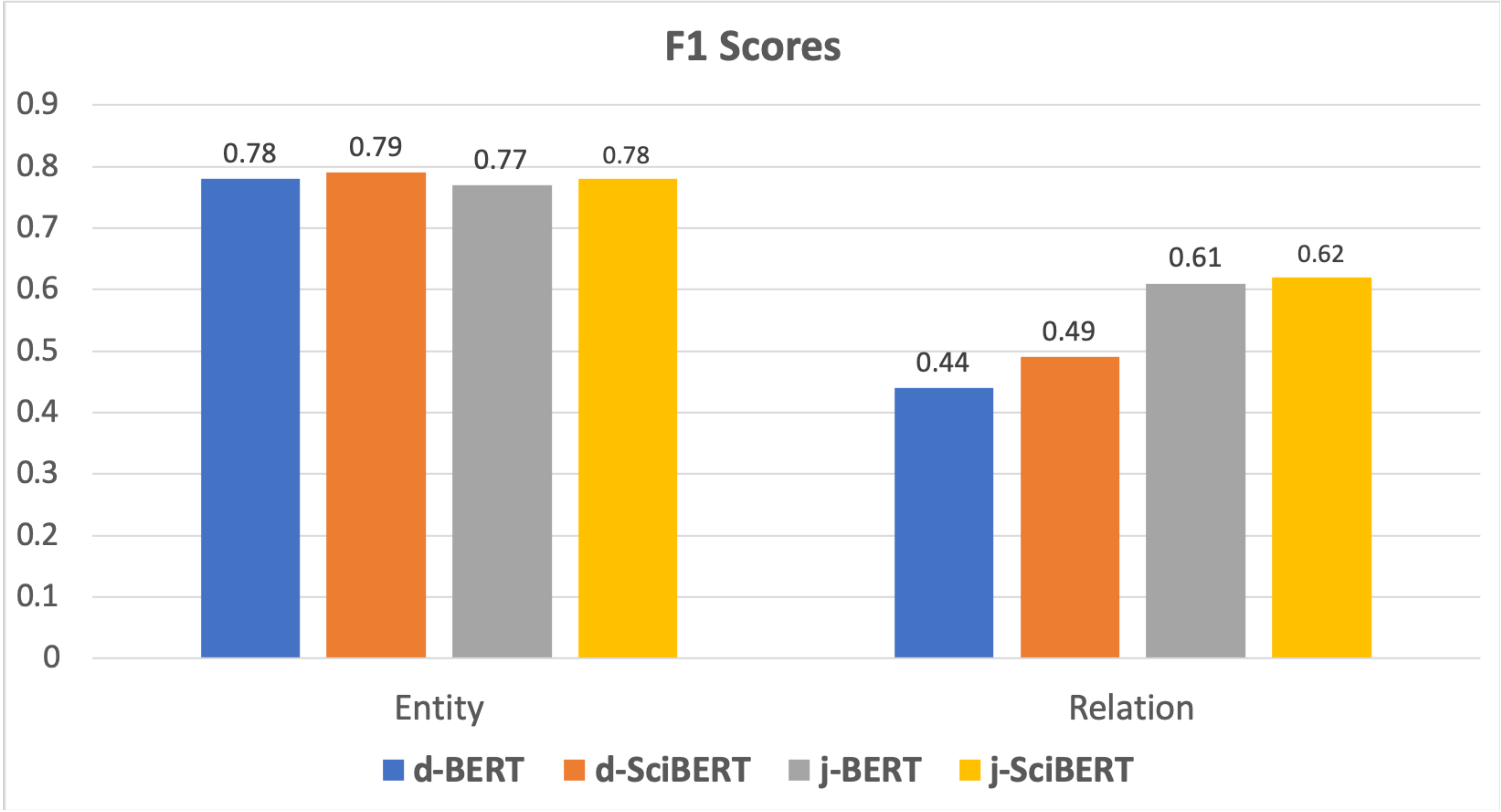
Full-text PDFs of Gene-Cancer Studies

$$\sum_{(D,R*,E*)\epsilon\mathcal{X}} \{\log \mathcal{P}(R^*|E,D) + \log \mathcal{P}(E^*|D)\}$$

<germline-mutation, risk> <germline-mutation, risk> ⋯ <germline-mutation, risk>



d – disjoint; j – joint

Thank you!

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