

A formalization of one of the main claims of “Cost-effectiveness analysis of pharmacogenomics-guided clopidogrel treatment in Spanish patients undergoing percutaneous coronary intervention” by Fragoulakis et al. 2019¹

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Abstract. Fragoulakis et al. claimed in previous work that pharmacogenomics-guided clopidogrel strategy represents a cost-effective treatment for patients undergoing PCI. We present here a formalization of that claim, stating that all things of class “pharmacogenomics guided clopidogrel therapy” that are in the context of a thing of class “patient undergoing PCI” generally have a relation of type “enables” to a thing of class “cost-effective treatment” in the same context.

Keywords: Patient undergoing PCI, pharmacogenomics-guided clopidogrel therapy, cost-effective treatment

1. Introduction

Fragoulakis et al. [2] state that “Our data show that pharmacogenomics-guided clopidogrel treatment strategy may represent a cost-effective choice compared with non-pharmacogenomics-guided strategy for patients undergoing PCI.”. We present here a formalization of the main scientific claim from this quote by using a semantic template called the super-pattern [1].

¹As RDF/nanopublication: http://purl.org/np/RAn15vsPJEVdJvjNKtBPo_oadtjeP9oc3Si-69FiJ4poQ

2. Formalization

Our formalization looks as follows:

CONTEXT-CLASS (“in the context of all. . .”):	patient undergoing PCI
SUBJECT-CLASS (“things of type. . .”):	pharmacogenomics guided clopidogrel therapy
QUALIFIER:	generally
RELATION-TYPE (“have a relation of type. . .”):	enables
OBJECT-CLASS (“to things of type. . .”):	cost-effective treatment

In the context class we use a new minted class “patient undergoing PCI” that is a subclass of “patient” (Q181600) from Wikidata and is related to the class “percutaneous coronary intervention” (Q2008344) from Wikidata. In the subject class, we use a new minted class “pharmacogenomics guided clopidogrel therapy” that is a subclass of “treatment” (Q179661) from Wikidata and is related to the class “pharmacogenomics” (Q1152227) and “clopidogrel” (Q410237) from Wikidata. In the object class we minted a new class “cost-effective treatment” that is a subclass of “treatment” (Q179661) from Wikidata and is related to the class “cost-effectiveness analysis” (Q1754768) from Wikidata.

3. RDF code

This is our formalization as a nanopublication in TriG format:

```
@prefix this: <http://purl.org/np/RAn15vsPJEVdJvjNKtBPO_oadtjeP9oc3Si-69FiJ4poQ> .
@prefix sub: <http://purl.org/np/RAn15vsPJEVdJvjNKtBPO_oadtjeP9oc3Si-69FiJ4poQ#> .
@prefix np: <http://www.nanopub.org/nschema#> .
@prefix dct: <http://purl.org/dc/terms/> .
@prefix nt: <https://w3id.org/np/o/ntemplate/> .
@prefix npx: <http://purl.org/nanopub/x/> .
@prefix xsd: <http://www.w3.org/2001/XMLSchema#> .
@prefix rdfs: <http://www.w3.org/2000/01/rdf-schema#> .
@prefix orcid: <https://orcid.org/> .
@prefix prov: <http://www.w3.org/ns/prov#> .
@prefix sp: <https://w3id.org/linkflows/superpattern/terms/> .

sub:Head {
  this: np:hasAssertion sub:assertion ;
  np:hasProvenance sub:provenance ;
  np:hasPublicationInfo sub:pubinfo ;
  a np:Nanopublication .
}
sub:assertion {
  sub:spi a sp:SuperPatternInstance ;
  rdfs:label "Pharmacogenomics-guided clopidogrel strategy represents a cost-effective treatment for patients undergoing PCI" ;
  sp:hasContextClass <http://purl.org/np/RA9pwySo43TIfbvPuhK4ZuisvMsDvZ6TeR5N6MNKft8Nw#patient_undergoing_PCI> ;
  sp:hasSubjectClass <http://purl.org/np/RA0xICL4ULhZr5mxC9yzStCBtpoETQGin6Vr-
Ns7JntA#pharmacogenomics_guided_clopidogrel_therapy> ;
  sp:hasQualifier sp:generallyQualifier ;
  sp:hasRelation sp:enables ;
  sp:hasObjectClass <http://purl.org/np/RAlfRfPak2jsyyVy4knjOmxQSYtociP8Cc007gemMtqQY#cost-effective_treatment> .
}
sub:provenance {
  sub:activity a sp:FormalizationActivity ;
  prov:used sub:quote , <https://pubmed.ncbi.nlm.nih.gov/30647444/> ;
  prov:wasAssociatedWith orcid:0000-0002-0519-7776 .
  sub:assertion prov:wasGeneratedBy sub:activity .
  sub:quote prov:value "Our data show that pharmacogenomics-guided clopidogrel treatment strategy may represent a cost-effective choice compared with non-pharmacogenomics-guided strategy for patients undergoing PCI." ;
  prov:wasQuotedFrom <https://pubmed.ncbi.nlm.nih.gov/30647444/> .
}
sub:pubinfo {
  sub:sig npx:hasAlgorithm "RSA" ;
  npx:hasPublicKey
  "MIGfMA0GCSqGSIb3DQEBQUAA4GNADCBiQKBgQCJlM78d80R+gFMoQB1IG3f7AbqqGOCiv4HmZd1cx1KgEWMUUpPsojFNvx84fC/TltoJ8F8JafnbhDXW2HM2
```

```

MhdK4yC04ROEV1vIgszjDicHfiqXvMqdPuMyQp4mmCEY7mUoeEW10mWZqjk+S9TnmiAQbFGcpExP8aosr2aTR7CSQIDAQAB" ;
npx:hasSignature
"ceQZgFgXgTd99RYcmWsqM1LCUciLc1lXuy6mfjgKhn0BfsMcesqIKR+51xx61fHD31tnz/bovIDh1YEPORGBe2PEvFMPvRRPd67B9slawepEP115tA7wmhkTOj
PrEUXISQaQu93NbpYMYSGnRx+Shv7jNxE+hPrxQw7fD6EgJr8=" ;
npx:hasSignatureTarget this: .
this: dct:created "2021-11-17T21:22:59.625+02:00"^^xsd:dateTime ;
dct:creator orcid:0000-0002-0519-7776 , orcid:0000-0002-7114-6459 ;
npx:introduces sub:spi ;
npx:supersedes <http://purl.org/np/RAB_yY8X4BUuS9HMBso8SvvPfbX31cb8cCv41SgfyMBew> ;
<https://w3id.org/linkflows/reviews/isUpdateOf> <http://purl.org/np/RAWCmrfeUUohlt01_7qFYoWgrYeonmX4FzAFboCSEoL-s> ;
nt:wasCreatedFromProvenanceTemplate <http://purl.org/np/RAElwmiOy0y039PlK9QkQ-wqbC3q-R2nXraP5huu8W39k> ;
nt:wasCreatedFromPubinfoTemplate <http://purl.org/np/RA2vCBXZf-icEcVRGhulJXugTGxpsV5yVr9yqCI1bQh4A> ,
<http://purl.org/np/RAA2MfQdBczmz9yVWjKLNbyfBNcwsMmOqcNUxkk1maIM> ,
<http://purl.org/np/RAjpbM1w3owYhJUBo3DtSuDlXsNAJ8cnGeWAutDVjuAuI> ;
nt:wasCreatedFromTemplate <http://purl.org/np/RAv68imZrEjfcP2rnEglhzoBqEVC0cQMtp9_1Za0BxNM4> .
}

```

The following nanopublications introduce the newly minted classes in TriG format.
This is the class definition of “patient undergoing PCI”:

```

@prefix this: <http://purl.org/np/RA9pwySo43TIfbvPuhK4ZuisvMsDvZ6TeR5N6MNKft8Nw> .
@prefix sub: <http://purl.org/np/RA9pwySo43TIfbvPuhK4ZuisvMsDvZ6TeR5N6MNKft8Nw#> .
@prefix np: <http://www.nanopub.org/nschema#> .
@prefix dct: <http://purl.org/dc/terms/> .
@prefix nt: <https://w3id.org/np/o/ntemplate/> .
@prefix npx: <http://purl.org/nanopub/x/> .
@prefix xsd: <http://www.w3.org/2001/XMLSchema#> .
@prefix rdfs: <http://www.w3.org/2000/01/rdf-schema#> .
@prefix orcid: <https://orcid.org/> .
@prefix prov: <http://www.w3.org/ns/prov#> .
@prefix skos: <http://www.w3.org/2004/02/skos/core#> .

sub:Head {
  this: np:hasAssertion sub:assertion ;
  np:hasProvenance sub:provenance ;
  np:hasPublicationInfo sub:pubinfo ;
  a np:Nanopublication .
}
sub:assertion {
  sub:patient_undergoing_PCI a <http://www.w3.org/2002/07/owl#Class> ;
  rdfs:label "patient undergoing PCI" ;
  rdfs:subClassOf <http://www.wikidata.org/entity/Q181600> ;
  skos:definition "patient undergoing percutaneous coronary intervention" ;
  skos:relatedMatch <http://www.wikidata.org/entity/Q2008344> .
}
sub:provenance {
  sub:assertion prov:wasAttributedTo orcid:0000-0002-0519-7776 .
}
sub:pubinfo {
  sub:sig npx:hasAlgorithm "RSA" ;
  npx:hasPublicKey
"MIgfMA0GCSqSIB3DQEBAQUAA4GNADCBiQKBgQCIJm78d80R+gFMOQB1IG3f7AbqqGOCiV4HmZdlcx1KgEWMUUpPsojFNvx84fC/TlctJ8F8JafnbhDXW
2HM2MhdK4yC04ROEV1vIgszjDicHfiqXvMqdPuMyQp4mmCEY7mUoeEW10mWZqjk+S9TnmiAQbFGcpExP8aosr2aTR7CSQIDAQAB" ;
  npx:hasSignature
"Iv6wAp5BYaY+ltBBEicPls8rQjacsBZifWaNxBQkJaoYJ5s/ejUrEiMXVvul4D+4baebbEm8rkT6vp336uDeencmLDiZzHZGL1ioFQTG1Bc//XYZYWkO/jcGRB
3HNolScLz1Fo/dWaB94+qrW9MSTi6eVmIY9YqjH+3mGY6HJRk=" ;
  npx:hasSignatureTarget this: .
  this: dct:created "2021-11-04T10:24:46.053+02:00"^^xsd:dateTime ;
  dct:creator orcid:0000-0002-0519-7776 , orcid:0000-0002-7114-6459 ;
  npx:introduces sub:patient_undergoing_PCI ;
  npx:supersedes <http://purl.org/np/RAuLZtfsHn3NGe0Md81LNvYmBseEtW9v1rVUVfJcPJYUE> ;
  <https://w3id.org/linkflows/reviews/isUpdateOf> <http://purl.org/np/RAuLZtfsHn3NGe0Md81LNvYmBseEtW9v1rVUVfJcPJYUE> ;
  nt:wasCreatedFromProvenanceTemplate <http://purl.org/np/RAI6zZawhaJ23Hzg4Ij1Pir6Take3ZQp-1S9skfBEwfQ> ;
  nt:wasCreatedFromPubinfoTemplate <http://purl.org/np/RA2vCBXZf-icEcVRGhulJXugTGxpsV5yVr9yqCI1bQh4A> ,
  <http://purl.org/np/RAA2MfQdBczmz9yVWjKLNbyfBNcwsMmOqcNUxkk1maIM> ,
  <http://purl.org/np/RAOGu9Lh0BD4tbIRB9RG6RGRa_ObDh75NTbIqaWgxxs8M> ;
  <http://purl.org/np/RAjpbM1w3owYhJUBo3DtSuDlXsNAJ8cnGeWAutDVjuAuI> ;
  nt:wasCreatedFromTemplate <http://purl.org/np/RAdpgrpigXtt8iPV9uOPf3wIT3qzOI8Sg2Q72CNV8g-Yo> .
}

```

This is the class definition of “pharmacogenomics guided clopidogrel therapy”:

```

@prefix this: <http://purl.org/np/RAOxICL4ULhZr5mxC9cyzStCBtpoETQGin6Vr-Ns7JNTA> .
@prefix sub: <http://purl.org/np/RAOxICL4ULhZr5mxC9cyzStCBtpoETQGin6Vr-Ns7JNTA#> .
@prefix np: <http://www.nanopub.org/nschema#> .
@prefix dct: <http://purl.org/dc/terms/> .
@prefix nt: <https://w3id.org/np/o/ntemplate/> .
@prefix npx: <http://purl.org/nanopub/x/> .

```

```

@prefix xsd: <http://www.w3.org/2001/XMLSchema#> .
@prefix rdfs: <http://www.w3.org/2000/01/rdf-schema#> .
@prefix orcid: <https://orcid.org/> .
@prefix prov: <http://www.w3.org/ns/prov#> .
@prefix skos: <http://www.w3.org/2004/02/skos/core#> .

sub:Head {
  this: np:hasAssertion sub:assertion ;
  np:hasProvenance sub:provenance ;
  np:hasPublicationInfo sub:pubinfo ;
  a np:Nanopublication .
}
sub:assertion {
  sub:pharmacogenomics_guided_clopidogrel_therapy a <http://www.w3.org/2002/07/owl#Class> ;
  rdfs:label "pharmacogenomics guided clopidogrel therapy" ;
  rdfs:subClassOf <http://www.wikidata.org/entity/Q179661> ;
  skos:definition "A clopidogrel therapy assisted by pharmacogenomics." ;
  skos:relatedMatch <http://www.wikidata.org/entity/Q1152227> , <http://www.wikidata.org/entity/Q410237> .
}
sub:provenance {
  sub:assertion prov:wasAttributedTo orcid:0000-0002-0519-7776 .
}
sub:pubinfo {
  sub:sig npx:hasAlgorithm "RSA" ;
  npx:hasPublicKey
  "MIGfMA0GCSSqIb3DQEBAAQUAA4GNADCBiQKBgQCJ1M78d80R+gFMOQB1IG3f7AbqqGOCiV4HmZd1cx1KgEWMUUpPsojFNvx84fC/TltoJ8F8JafnbhDXW2HM2
  MhdK4yC04ROEV1vIgszjDichFiqXvMqPuMyQp4mmCEY7mUoeEW10mWZqjk+S9TnmIAQbFGcpExp8aosr2aTR7CSQIDAQAB" ;
  npx:hasSignature
  "QNiCAE5wfsq1p8Z7J+KLQwAlpbm5/VZFeRJe6JKkIB6TvXtd102KOTDYMpZys15bU9yibaKOA/7YRQnaf6oTbgOmaT1mV5+zffRj15SG+z+4A1R7HLIfr2G2x
  9Z4kz55rQL+AQbvYgkDXiVMSsbdJdraQ5t/SBCJcEHOh2xuQ=" ;
  npx:hasSignatureTarget this: .
  this: dct:created "2021-11-04T11:02:34.246+02:00"^^xsd:dateTime ;
  dct:creator orcid:0000-0002-0519-7776 , orcid:0000-0002-7114-6459 ;
  npx:introduces sub:pharmacogenomics_guided_clopidogrel_therapy ;
  npx:supersedes <http://purl.org/np/RA4BJq9pLse6z1BRbZIOgARyflzOY9Qw3ix3lsHcazOE> ;
  <https://w3id.org/linkflows/reviews/isUpdateOf> <http://purl.org/np/RAvOAYeg-J8ynmZnrkCgg5XqGuqRo-dXcGFVgDLxtY6ck> ;
  nt:wasCreatedFromProvenanceTemplate <http://purl.org/np/RAi6zZAwahaJ23Hzg4Ij1Pir6Take3ZQp-LS9skfBEwfQ> ;
  nt:wasCreatedFromPubinfoTemplate <http://purl.org/np/RA2vCBXZf-icEcVRGhulJXugTGxpsV5Yr9yqCI1bQh4A> ,
  <http://purl.org/np/RAA2MfgdBczmz9yVWjKLNbyfBNcwsMmOqCNuxkklmaIM> ,
  <http://purl.org/np/RAjpbM1w3owYhUBo3DtsuDL1XsNAJ8cnGeWautDVjuAuI> ;
  nt:wasCreatedFromTemplate <http://purl.org/np/RADpgRpigXtt8iPV9uOpf3wIT3qzOI8Sg2Q72CNV8g-Yo> .
}

```

This is the class definition of “cost-effective treatment”:

```

@prefix this: <http://purl.org/np/RAlfRfPak2jsyyVy4knjOmxQSYtociP8Cc007gemMtqQY> .
@prefix sub: <http://purl.org/np/RAlfRfPak2jsyyVy4knjOmxQSYtociP8Cc007gemMtqQY#> .
@prefix np: <http://www.nanopub.org/nschema#> .
@prefix dct: <http://purl.org/dc/terms/> .
@prefix nt: <https://w3id.org/np/ontology#> .
@prefix npx: <http://purl.org/nanopub/x/> .
@prefix xsd: <http://www.w3.org/2001/XMLSchema#> .
@prefix rdfs: <http://www.w3.org/2000/01/rdf-schema#> .
@prefix orcid: <https://orcid.org/> .
@prefix prov: <http://www.w3.org/ns/prov#> .
@prefix skos: <http://www.w3.org/2004/02/skos/core#> .

sub:Head {
  this: np:hasAssertion sub:assertion ;
  np:hasProvenance sub:provenance ;
  np:hasPublicationInfo sub:pubinfo ;
  a np:Nanopublication .
}
sub:assertion {
  sub:cost-effective_treatment a <http://www.w3.org/2002/07/owl#Class> ;
  rdfs:label "cost-effective treatment" ;
  rdfs:subClassOf <http://www.wikidata.org/entity/Q179661> ;
  skos:definition "cost-effective treatment" ;
  skos:relatedMatch <http://www.wikidata.org/entity/Q1754768> .
}
sub:provenance {
  sub:assertion prov:wasAttributedTo orcid:0000-0002-0519-7776 .
}
sub:pubinfo {
  sub:sig npx:hasAlgorithm "RSA" ;
  npx:hasPublicKey
  "MIGfMA0GCSSqIb3DQEBAAQUAA4GNADCBiQKBgQCJ1M78d80R+gFMOQB1IG3f7AbqqGOCiV4HmZd1cx1KgEWMUUpPsojFNvx84fC/TltoJ8F8JafnbhDXW2HM2Mhd
  K4yC04ROEV1vIgszjDichFiqXvMqPuMyQp4mmCEY7mUoeEW10mWZqjk+S9TnmIAQbFGcpExp8aosr2aTR7CSQIDAQAB" ;
  npx:hasSignature
  "f+XJLoVxSGHxnuQYxbgd+cAlljMEdnPppQ011jalPaJlNUREPKWRB5A9mshvEuV1TWGzHfz1wEL8FiguHgg7YU7Jlba1pb8qA98/MFkwtXeYzIjwOgmUFUrSIBQF0

```

```

cEVX5OV8D3nzwwa+Y2glBes1lpIkSRgAH4b3KMy8+PbNBg=" ;
  npx:hasSignatureTarget this: .
  this: dct:created "2021-11-04T10:28:39.058+02:00"^^xsd:dateTime ;
  dct:creator orcid:0000-0002-0519-7776 , orcid:0000-0002-7114-6459 ;
  npx:introduces sub:cost-effective_treatment ;
  npx:supersedes <http://purl.org/np/RAjD4-Q2kO_cIUE52rde2uWbV3RtuCR90geXW90il2YX4> ;
  <https://w3id.org/linkflows/reviews/isUpdateOf> <http://purl.org/np/RAjD4-Q2kO_cIUE52rde2uWbV3RtuCR90geXW90il2YX4> ;
  nt:wasCreatedFromProvenanceTemplate <http://purl.org/np/RAi6zZAwhaJ23Hzg4Ij1Pir6Take3ZQp-1S9skfBEwfQ> ;
  nt:wasCreatedFromPubinfoTemplate <http://purl.org/np/RA2vCBXZf-icEcVRGhulJXugTGxpsV5yVr9yqCI1bQh4A> ,
  <http://purl.org/np/RAA2MfqdBczmz9yVWjKLNbyfBNcwsMmOqcNuxkk1maIM> ,
  <http://purl.org/np/RAOGu9Lh0BD4tbIRB9RG6RGRA_ObDh75NTbIqaWgxxs8M> ;
  <http://purl.org/np/RAjpbMlw3owYhJUBo3DtsuDlXsNAJ8cnGeWAutDVjuAuI> ;
  nt:wasCreatedFromTemplate <http://purl.org/np/RAdpgRpigXtt8iPV9uOPf3wIT3qzOI8Sg2Q72CNV8g-Yo> .
}

```

References

- [1] C.I. Bucur, T. Kuhn, D. Ceolin and J. van Ossenbruggen, Expressing high-level scientific claims with formal semantics, in: *Proceedings of the 11th Knowledge Capture Conference*, 2021. doi:[10.1145/3460210.3493561](https://doi.org/10.1145/3460210.3493561).
- [2] V. Fragoulakis, M. Bartsakoulia, X. Díaz-Villamarín, K. Chalikiopoulou, K. Kehagia, J.G.S. Ramos, L.J. Martínez-González, M. Gkotsi, E. Katrali, E. Skoufas, A. Vozikis, A. John, B.R. Ali, S. Wordsworth, C.L. Dávila-Fajardo, T. Katsila, G.P. Patrinos and C. Mitropoulou, Cost-effectiveness analysis of pharmacogenomics-guided clopidogrel treatment in Spanish patients undergoing percutaneous coronary intervention, *Pharmacogenomics J.* **19**(5) (2019), 438–445. doi:[10.1038/s41397-019-0069-1](https://doi.org/10.1038/s41397-019-0069-1).