



The importance of national and international collaboration in adult congenital heart disease: A network analysis of research output[☆]



Melanie Iris Orwat^a, Aleksander Kempny^{b,c}, Ulrike Bauer^d, Michael A. Gatzoulis^{b,c}, Helmut Baumgartner^a, Gerhard-Paul Diller^{a,b,c,*}

^a Division of Adult Congenital and Valvular Heart Disease, Department of Cardiovascular Medicine, University Hospital Münster, Münster, Germany

^b Imperial College of Science and Medicine, London, UK

^c Adult Congenital Heart Centre and Centre for Pulmonary Hypertension, NIHR Cardiovascular and Respiratory Biomedical Research Unit, Royal Brompton Hospital, London, UK

^d National Register for Congenital Heart Defects, Berlin, Germany

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ABSTRACT

Background: The determinants of adult congenital heart disease (ACHD) research output are only partially understood. The heterogeneity of ACHD naturally calls for collaborative work; however, limited information exists on the impact of collaboration on academic performance. We aimed to examine the global topology of ACHD research, distribution of research collaboration and its association with cumulative research output.

Methods and results: Based on publications presenting original research between 2005 and 2011, a network analysis was performed quantifying centrality measures and key players in the field of ACHD. In addition, network maps were produced to illustrate the global distribution and interconnected nature of ACHD research. The proportion of collaborative research was 35.6% overall, with a wide variation between countries (7.1 to 62.8%). The degree of research collaboration, as well as measures of network centrality (betweenness and degree centrality), were statistically associated with cumulative research output independently of national wealth and available workforce. The global ACHD research network was found to be scale-free with a small number of central hubs and a relatively large number of peripheral nodes. In addition, we could identify potentially influential hubs based on cluster analysis and measures of centrality/key player analysis.

Conclusions: Using network analysis methods the current study illustrates the complex and global structures of ACHD research. It suggests that collaboration between research institutions is associated with higher academic output. As a consequence national and international collaboration in ACHD research should be encouraged and the creation of an adequate supporting infrastructure should be further promoted.

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1. Introduction

Over recent decades Adult Congenital Heart Disease (ACHD) has emerged as an important sub-speciality in cardiology. This is due to a steady increase in numbers and complexity of patients with congenital heart lesions reaching adulthood which comes with evolving cardiac and non-cardiac health care needs [1–3]. These patients are by and large not cured and most require specialized life-long follow-up [4]. The rising importance of the ACHD field is reflected not only by the increasing number of tertiary centers in Europe, North America and the rest of the world [5,6], but also by the establishment and endorsement of ACHD training curricula by national and international cardiology

societies [7]. Furthermore, this relatively young branch of cardiology requires constant research efforts to keep pace with the aging and evolving patient population, to improve our knowledge and ultimately to enable ACHD patients to achieve their full life potential. Recently, we reported data on contemporary ACHD research and provided an overview of global centers and their ACHD research activity [8]. While providing a first insight into the field, this former analysis was not designed to investigate the contribution of collaborative research in ACHD. This was mainly due to the nature of data employed. We, herewith, expand on our previous work and investigate the status and importance of collaboration in ACHD research. Our underlying hypothesis is that voluntary collaboration between institutions leads to synergistic effects, improves efficiency and ultimately is reflected by higher academic output of those centers involved. To test this hypothesis we use a richer dataset (including the affiliation of all authors) and methods of social network analysis. Specifically, we describe the degree and global distribution of research collaboration and explore the association between collaborative research or interaction between actors and cumulative research output over our study period.

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* Corresponding author at: Division of Adult Congenital and Valvular Heart Disease, Department of Cardiovascular Medicine University Hospital of Münster, Albert-Schweitzer-Str. 33, 48149 Münster, Germany.

E-mail address: gerhard.diller@ukmuenster.de (G.-P. Diller).

2. Methods

2.1. Data sources

The strategy for identifying relevant ACHD publications has been previously described [8]. Briefly, the PubMed database was searched for keywords based on MeSH phrases relevant to congenital heart defects and for terms identified by the authors from contemporary ACHD guidelines. The identified articles were first filtered automatically and subsequently manually to ensure that only original ACHD papers published in English between 2005 and 2011 were included. Papers including only children were excluded, as were those publications describing only laboratory based methods or animal research without transfer to human subjects. Based on the identified list of papers a Scopus Database query (<http://www.scopus.com/>) was performed to obtain the affiliations of all authors involved. We studied research at the macro- and micro-levels; therefore publications were not linked to individual institutions but rather assigned to city and country of origin. To gain some insight into the output and interconnection of different institutions, we investigated research output of individual authors and linked this to relevant geographic locations and affiliated institutions.

Impact factor (IF) data was assigned to each publication as described previously. Additional data on the population, the gross domestic product (GDP) and the number of practicing physicians were obtained from Word Bank (<http://www.worldbank.org/>) for the year 2010.

2.2. German national registry for congenital heart disease publications

Based on data from the German Competence Network and National Register for Congenital Heart Disease (data on file) we aimed to quantify the number of institutions involved in collaborative research based on this infrastructure and to delineate its potential to foster collaborative work.

2.3. Network analysis

To describe the relationship between publishing institutions and to illustrate how individual actors (nodes) are embedded in the global research network standard methods of social network analysis were employed. To this end a directed network was build. Edges (ties) linking two cities were constructed such that the origin of the link is at the workplace of the first author with connections directed towards all of the co-author institutions' places. The ties were weighted by the cumulative IF of the respective link. In addition, a weighted directed network was also constructed based on authors' names and initials. The relative importance of a node was quantified using various metrics. One approach to identify the most central nodes is to study the contribution of individual actors to the overall coherence of the network. Following this concept, *centrality* aims to identify the most influential/important nodes within a network. Different interpretations of "importance" exist and various metrics have been proposed to assess centrality. Commonly utilized implementations are betweenness and the quantification of the so called degrees of a particular node. *Betweenness centrality* quantifies the alleged importance of a node by assessing its location within the network. Specifically, a particular node is considered important if it helps to connect many other nodes, that is, if it forms part of the shortest path between a large fraction of the nodes of the network. Formally this is measured as the proportion of the shortest paths between all nodes passing through the node of interest as follows:

- Calculate the shortest path between all pairs of nodes
- Calculate the fraction of shortest paths for all pair of nodes that include the node of interest
- Add up the fractions of shortest paths passing through the node of interest.

The logic behind this approach is that a node with a high betweenness value is responsible for connecting many other actors (at least cost) and thus could be considered to be influential. *Degree centrality*, in contrast, quantifies the number of nodes connected directly to a node of interest. The rationale is that more connected nodes are potentially more influential compared to *less connected ones*. This is analogous to considering people with many connections (friends) to be more important (or popular) compared to those with fewer connections. Formally this parameter is measured by adding up the number of direct links for each node.

As the network utilized in the current study is directed, two different measures of degree centrality exist: in-degrees refer to the number of links a node of interest receives, while out-degrees quantify the number of ties directed towards neighboring nodes. The measurement of betweenness centrality and the number of degrees was performed with UCINET Version 6.5.1.6 (UCINET 6 For Windows: Software for Social Network Analysis (2002) by S. P. Borgatti, M. G. Everett, L. C. Freeman; Analytic Technologies, Lexington, KY, USA). Fig. 1 provides an intuitive illustration of the concepts underlying betweenness and degree centrality; however, for a formal (mathematical) definition of the parameters we refer to Ref. [9–11]. Graphical representations of the research network were created using the R and Gephi version 0.8.2.β. To visualize collaboration in geographic space, maps of co-authorship were produced by connecting the place of affiliation of the first author with that of all co-authors. Coordinates were connected by great circles with the use of R and the geosphere package.

2.4. Key player analysis

Another fundamental approach to identify the most influential nodes is to selectively disable or manipulate nodes and assess the impact on the flow of information within the network [12,13]. This approach is implemented in key player analysis. *These analyses essentially build on the concepts discussed above for between and degree centrality by using alternative algorithms*. The two fundamentally available approaches proposed in the literature are (i) identifying a small number of influential nodes with the aim of disturbing the coherence or fragmenting the network (disruption approach). Alternatively, (ii) one aims to identify a set of maximally connected nodes and target those nodes for interventions within the network (influence approach). Both concepts are implemented in the KeyPlayer software package (Version 1.45, Analytic Technologies, Boston, USA) and are used here to supplement the results of conventional methods of social network analysis.

2.5. Statistical correlation analysis

As most parameters assessed were not normally distributed, the preferred approach to test for an association between network metrics and research output was the use of non-parametric Spearman rank correlation analyses. To correct for the potential influence of confounders including national wealth, population and the size of the medical workforce multivariate correlation analyses were performed on log-transformed variables using robust regression methods. For all analyses a *p*-value < 0.05 (two-sided) was considered statistically significant. R Version 3.0.2 was used for all analyses [14].

3. Results

3.1. Collaborative research – cities as units of analysis

Overall, 2172 publications were included in the analysis; 37.3% of those were collaborative. Of the collaborative manuscripts, 69.5% involved a national collaborative partner. Over time, a slow increase in the percentage of collaborative research was seen, with an increase from 35.6% collaborative publications in 2005 to 41.1% in 2011.

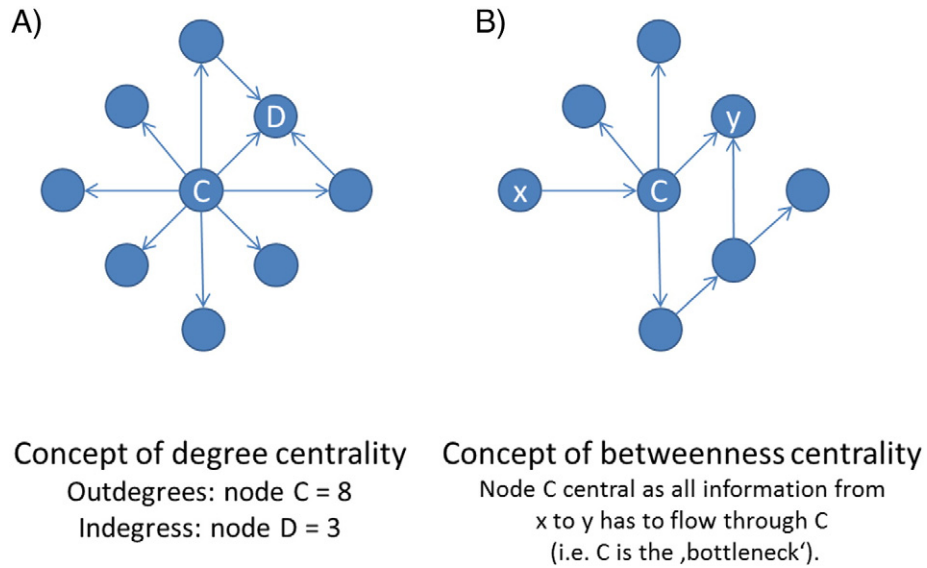


Fig. 1. Basic overview over the concepts of degree and betweenness centrality based on unweighted binary networks. A) Degree centrality determines the number of nodes directly connected to the node of interest (C in this case). In the case of directed networks (used in this article) a distinction between outgoing and incoming connections has to be made. By counting the number of outgoing ties, C has the highest out-degree, with 8 connections, while all other nodes have at most 2 outgoing connections. For incoming ties, D has the highest in-degree with 3 incoming connections. B) Betweenness centrality quantifies the proportion of connections between all combinations of nodes passing through the node of interest [9].

There was a wide variation between countries in the percentage of collaborative research. The range was from 7.1 % to 62.8% for countries with at least 10 collaborative publications during the study period. As

illustrated in Fig. 2, countries with high levels of collaborative research included the Netherlands, Norway and Austria. The percentage of collaborative research or national collaborative research was, however,

Land	Nb. publications	% collaborative publications	% of collaboration national	national collaborations % of total research
1 Netherlands	145	62.8%	90.1%	56.6%
2 Norway	18	61.1%	72.7%	44.4%
3 Austria	10	60.0%	16.7%	10.0%
4 Mexico	12	50.0%	33.3%	16.7%
5 Canada	109	49.5%	46.3%	22.9%
6 Germany	218	44.5%	77.3%	34.4%
7 Sweden	16	43.8%	57.1%	25.0%
8 Israel	21	42.9%	77.8%	33.3%
9 Italy	123	42.3%	71.2%	30.1%
10 United Kingdom	160	38.8%	35.5%	13.8%
11 United States	456	38.4%	89.7%	34.4%
12 France	66	37.9%	64.0%	24.2%
13 Denmark	24	37.5%	55.6%	20.8%
International Average		37.3%	69.5%	25.9%
14 Greece	22	36.4%	37.5%	13.6%
15 South Korea	40	35.0%	78.6%	27.5%
16 Belgium	55	34.5%	42.1%	14.5%
17 Australia	33	33.3%	100.0%	33.3%
18 Switzerland	40	32.5%	53.8%	17.5%
19 Japan	111	31.5%	77.1%	24.3%
20 Taiwan	37	27.0%	100.0%	27.0%
21 Poland	36	25.0%	77.8%	19.4%
22 Iran	20	25.0%	20.0%	5.0%
23 Turkey	38	23.7%	100.0%	23.7%
24 China	124	22.6%	60.7%	13.7%
25 Spain	20	20.0%	25.0%	5.0%
26 Hong Kong	28	17.9%	0.0%	0.0%
27 Brazil	28	14.3%	25.0%	3.6%
28 India	53	9.4%	60.0%	5.7%
29 Portugal	14	7.1%	100.0%	7.1%
30 Thailand	14	7.1%	100.0%	7.1%

Fig. 2. Percentage of collaborative publications by country in order of decreasing proportion. Percentage of collaborative publications refers to collaborative publications in % of all publications, while national collaborative research is limited to the % of research involving a partner from a domestic national city.

Table 1

Correlation analyses: association between country size or national wealth and proportion of collaborative research.

Dependant variable	Independent variable	ρ^a	p^a
% collaborative research	GDP 2010 (US\$)	0.15	0.29
% collaborative research	Population 2010 (10^6)	-0.10	0.48
% national collaborative research	GDP 2010 (US\$)	0.11	0.47
% national collaborative research	Population 2010 (10^6)	0.08	0.59

^a Spearman rank correlations.

not statistically correlated to country size or GDP of the respective country (Table 1; $p > 0.05$ for all parameters).

A geographic representation of research collaborations on a global scale is presented in Fig. 3, while Figs. I and II in the online appendage section show similar maps for Europe and North America. The maps illustrate the intercontinental links and allow for the identification of major hubs in this world-wide network.

3.2. Network characteristics and topological properties

Descriptive network statistics are provided in Table 2 for the city-based network. The table shows that publications originating from 542 geographical places with 2118 connections between cities were included. For the author based network the number of nodes was 7520 with 10,158 connections between authors. The data in Table 2 also illustrates that the current network is sparse with a relatively low average path length of only 4.4. This suggests that – on average – every node within the network can be reached with the aid of only approx. 4 intermediary nodes. Together with the low overall density of the graph and its substantially higher clustering coefficient (1.47) compared to that of a random Erdős–Rényi graph [15] of similar size and density (0.026) this is consistent with a small world network [16,17]. Node linkage data shown in Fig. III (online appendix) illustrates that degrees follow a power law distribution consistent with a scale-free network [18]. This type of network is characterized by a large number of relatively insignificant nodes and a small number of highly connected nodes (hubs), dominating the structure [19].

Table 3 shows the results of the centrality measures for the entire network. It highlights the central position of some well-established ACHD research institutions (such as Amsterdam, Boston, London and Toronto) but also illustrates the high degree centrality values calculated

Table 2

Descriptive network statistics for the city-based network. SD = standard deviation.

Network characteristic	Value
Size (nodes)	542
Size (edges)	2118
Average path length (\pm SD)	4.4 ± 1.6
Diameter	10
Average clustering coefficient (weighted)	$1.47 (0.80)$
Degree (out-degree)	1.31
Degree (in-degree)	0.47
Density (\pm SD)	0.024 ± 0.667
Assortativity	-0.045
Betweenness centrality (\pm SD)	469.9 ± 1790.7
Betweenness centrality (normalized, \pm SD)	0.160 ± 0.611

for various other cities from the Netherlands. For example 6 Dutch cities were among the top-10 locations with the highest in-degrees worldwide.

The results of the key player analysis are presented in Table 4. It supports the notion of conventional network analysis that a relatively small number of distinct nodes act as hubs connecting the network.

To investigate the statistical association between proportions of collaborative research or network centrality and research output correlation analyses were performed using non-parametric and robust linear (parametric) regression methods. The results of these analyses are presented in Table 5. A significant association between network centrality (in-degree, out-degree and betweenness) and cumulative research output was found, using both non-parametric univariate analysis and multivariate regression analysis, adjusting for GDP and number of physicians.

To visualize the interaction between actors in the city- and author-based research network node-link diagrams were created. Fig. 4 presents the graph drawing for the city-based network. The circles represent individual cities, with the area of the respective circle corresponding to degree centrality (a measure of “importance”), while the links are weighted by the cumulative impact factor of the individual connection. Clusters of nodes are color-coded automatically based on modularity class (a community detection algorithm implemented in Gephi) [20]. These analyses identified hierarchical structures and clusters of closely connected cities. Fig. 5 is based on the individual author data. It allows the identification of individual

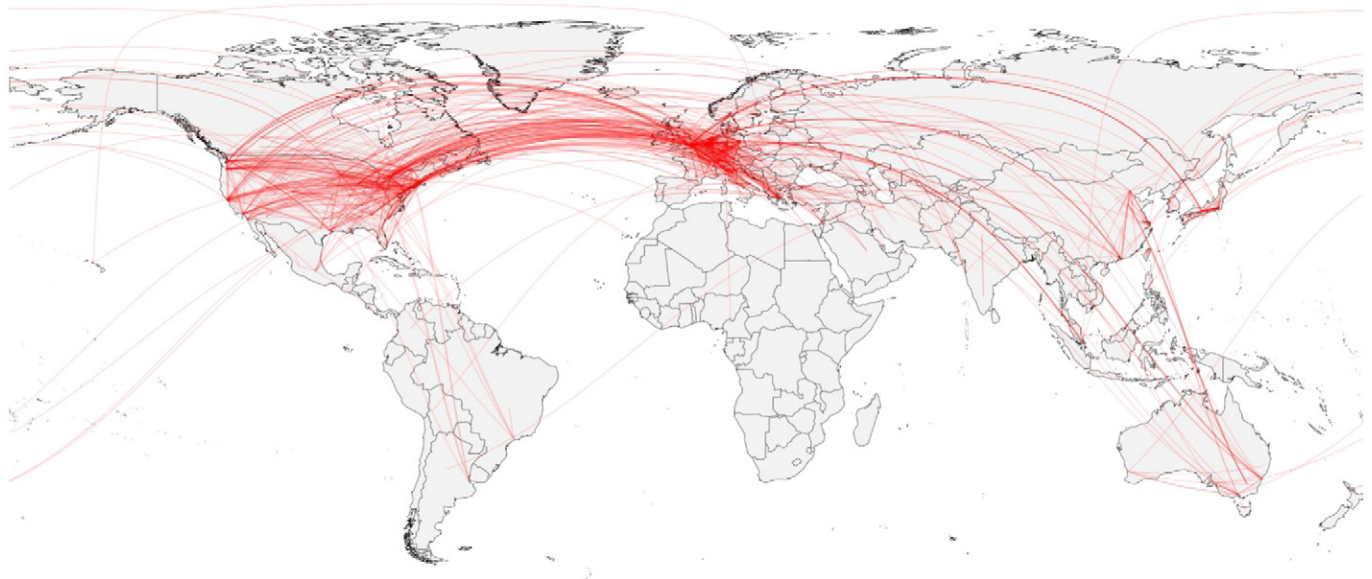


Fig. 3. Geographical representation of research links. Each line connects the place of affiliation of the first author to all co-authors. Connections are drawn as great circles (i.e. the shortest path between two sets of coordinates on the surface of the globe).

Table 3
Network statistics.

Rank	City, country	Out-degrees
1	<i>Amsterdam, Netherlands</i>	720.8
2	London, UK	426.3
3	Toronto, Canada	284.8
4	Boston, USA	233.4
5	<i>Rotterdam, Netherlands</i>	219.4
6	Montreal, Canada	214.8
7	Dijon, France	197.5
8	<i>Groningen, Netherlands</i>	191.8
9	Seattle, USA	187.0
10	Clamart, France	175.7

Rank	City, country	In-degrees
1	London, UK	267.0
2	<i>Utrecht, Netherlands</i>	261.5
3	Boston, USA	219.3
4	<i>Leiden, Netherlands</i>	193.6
5	<i>Groningen, Netherlands</i>	182.6
6	<i>Amsterdam, Netherlands</i>	172.8
7	<i>Nijmegen, Netherlands</i>	169.0
8	Philadelphia, USA	167.9
9	<i>Rotterdam, Netherlands</i>	133.8
10	New York, USA	117.1

Rank	City, country	Betweenness ^a
1	London, UK	9.77
2	Boston, USA	4.38
3	Toronto, Canada	4.27
4	New York, USA	3.46
5	Dallas, USA	2.39
6	Chiba, Japan	2.34
7	Hong Kong, China	2.34
8	Baltimore, USA	2.29
9	Milan, Italy	2.19
10	Portland, USA	2.14

The top 10 lists of cities based on degree and betweenness centrality (sorted in order of decreasing formal network analysis importance) are provided. Cities from the Netherlands are highlighted in *italics* as these are overrepresented in this analysis. For details on the measures used see the [Methods](#) section.

^a Betweenness measures are normalized.

centers based on affiliated authors and illustrates the relatively large number of peripheral only loosely connected nodes.

Based on data from publications emerging from the German National Register for Congenital Heart Defects between 2004 and 2014 we assessed the number of collaborating institutions. Overall 91 publications emerged from the Register, with a median number of 13 institutions (interquartile range 6 to 22). Only 12 publications had fewer than 3 collaborating centers, while 52 (57.1%) had more than 10 involved institutions.

Table 4

Results of the key player analysis with the top-10 cities presented for each metric of node importance. For details please refer to the [Methods](#) section and Ref. [12]. Fragmentation refers to disrupting the network such that a maximal number of unconnected sub-networks are created. The distance criterion is based on the concept of deleting nodes that maximally increase transmission distances in the network. Cities are ranked by cumulative impact factors over the study period.

Disruption approach				Influence approach	
Fragmentation		Distance weighted criterion		Distance weighted criterion	
Rank	City	Rank	City	Rank	City
1	London, UK	1	London, UK	1	London, UK
2	Toronto, Canada	2	Toronto, Canada	2	Milan, Italy
3	Boston, USA	3	Boston, USA	3	Beijing, China
4	New York, USA	4	Amsterdam, Netherlands	4	Zurich, Switzerland
5	Milan, Italy	5	New York, USA	5	Padua, Italy
6	Shanghai, China	6	Milan, Italy	6	Istanbul, Turkey
7	Freiburg, Germany	7	Beijing, China	7	Zabrze, Poland
8	Bethesda, USA	8	Shanghai, China	8	Detroit, USA
9	Padua, Italy	9	Padua, Italy	9	Yokohama, Japan
10	Yokohama, Japan	10	Yokohama, Japan	10	Winnipeg, Canada

Table 5
Correlation analyses.

A) Association between proportion of collaborative research and cumulative research output ^a adjusted for country size.			
Dependant variable	Independent variable	rho ^b	p ^b
Cumulative impact factor/population (10 ⁶)	% collaborative research	0.32	0.02
	% national collaborative research	0.27	0.07
Cumulative impact factor/population (10 ⁶)	In-degree centrality	0.74	<0.001
	Out-degree centrality	0.73	<0.001
	Betweenness centrality	0.73	<0.001

B) Association between network centrality and cumulative research output. ^c Multivariate linear regression analysis			
Dependant variable	Independent variables	r	p ^d
Cumulative impact factor	In-degree centrality	1.308	<0.001
	Betweenness centrality	0.140	0.007
	Number of physicians	0.294	0.10
Cumulative impact factor/population (10 ⁶)	GDP 2010 (US\$)	0.341	0.24
	In-degree centrality	1.525	<0.001
	Betweenness centrality	0.234	<0.001
	Number of physicians	−0.457	0.036
	GDP 2010 (US\$)	0.011	0.97

^a \sum_{2005}^{2011} impact factor.

^b Spearman rank correlations.

^c \sum_{2005}^{2011} impact factor; non-normally distributed, log transformed variable.

^d Linear regression with heteroskedasticity corrected standard errors.

4. Discussion

The current study illustrates the complex network structure underlying research in ACHD and highlights how different cities, authors and institutions are embedded in this interconnected dynamic global network. The main findings of our study are that national and international research collaboration is common but unevenly distributed between places and nations. While most publications are based on collaborative research efforts in countries such as the Netherlands or Scandinavia, this is clearly not the case for other nations with an established ACHD research track record. In addition, while some countries have a large proportion of collaboration both nationally and internationally, others are characterized by predominantly international collaboration. This is especially the case for the UK, where we found that only approx. 14% of all publications originated from more than one city in the country. One can only speculate about the reason for this finding, but it may relate to the prevailing hierarchically organized health care system and an old system of independent practice that may not foster a collaborative approach to research. In addition, recent

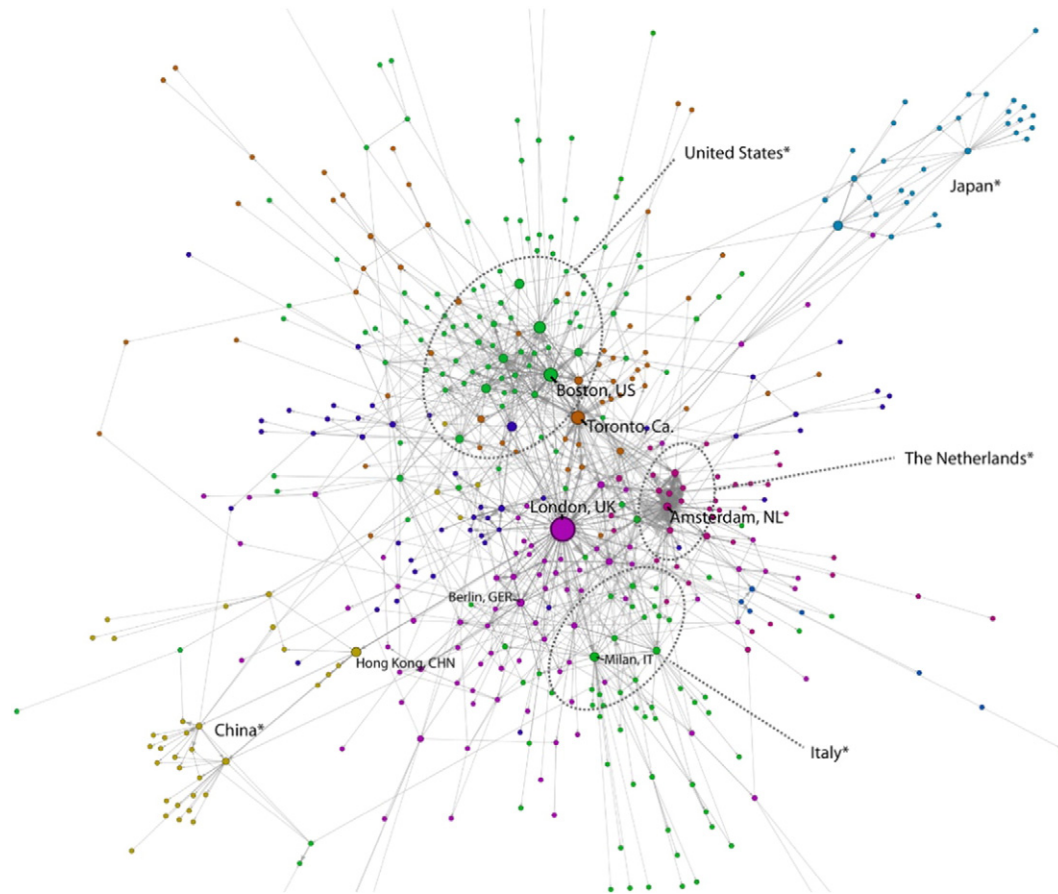


Fig. 4. Network graph (Force Atlas representation) of the city-based data set. The size of the nodes corresponds to the degree centrality of the node, the weight assigned to the ties corresponds to the cumulative impact factor of the particular link. Node clusters are colored automatically based on modularity. The labels and dotted ellipses were added manually to illustrate the nature of some of the visually more prominent nodes.

attempts to reform the congenital heart disease framework, which has been top-down and fragmented, may have been an obstacle towards fostering collaboration and for creating voluntary research associations.

Based on a visual inspection of Fig. 2 it would appear that smaller countries have a higher degree of collaboration, maybe based on personal acquaintance, a shared training history and the ease of personal communication. Statistically, however, we could not establish an association between country population or national wealth and the proportion of collaborative research. It is therefore likely that unobserved variables such as organization of clinical or academic structures and local mentality are – at least – in part responsible for this finding. Regardless of the underlying reasons, the variation in the proportion of collaborative research is likely to be important as we could establish an independent association between the degree of embeddedness in the global research network and general research output. This finding is intuitively plausible as increased collaboration should contribute to improved efficiency, taking advantage of synergistic effects between centers. The observation that national collaboration is related to research output is also consistent with a previous observation that especially the Netherlands and Canada are leading in terms of cumulative research output per national population or wealth [8]. This suggests that in addition to adequate financial resource and specialized workforce, the presence of centers of excellence and a tradition of academic research [21], collaboration is a major determinant of scientific results. Furthermore, at least theoretically collaborative relationships improve efficiency based on synergistic effects.

While Fig. 3 highlights that ACHD research is truly global, further analyses and network visualizations showed that the ACHD research network exhibits characteristics of small world, scale free networks.

This type of network is characterized by a limited number of prominent nodes acting as hubs and a large number of only loosely connected more peripheral nodes [22,19]. Network theorists have related these networks to a phenomenon known as “preferential attachment” [19]. Previous theoretical and modeling work suggests that these types of networks ensue in the setting of dynamic, growing networks where new nodes connect preferentially to the most influential incumbent structures, therefore this structure relates to the evolution of the network [19]. The fact that we identified this type of network in ACHD research is relevant for two reasons. Firstly, it is consistent with the development of the ACHD field over the last few decades, representing an area of rapid growth, catalyzed by a few eminent figures that attracted, trained and supported junior colleagues [23–25]. Secondly, this finding has possible future implications, suggesting that well connected, centrally located (in the formal network analysis sense) and influential institutions are likely to expand further and be advantaged in attracting high quality publications and gifted colleagues in the future. For an in-depth discussion of elements of network theory in the medical field see Ref. [26].

Regulatory agencies are increasingly turning their attention to the ACHD field, aiming to consolidate and regulate services. Beyond the obvious target of improving clinical service quality, augmenting research output is quoted as a possible benefit of such an approach. The Review of Adult Congenital Heart Disease Services in England, for example quotes as one of its aims, to “...[create a] network of specialist centers collaborating in research and clinical development, encouraging the sharing of knowledge across the network” [27]. However, research institutions are embedded in a large and decentralized global network that has emerged and evolved over the years without centralistic

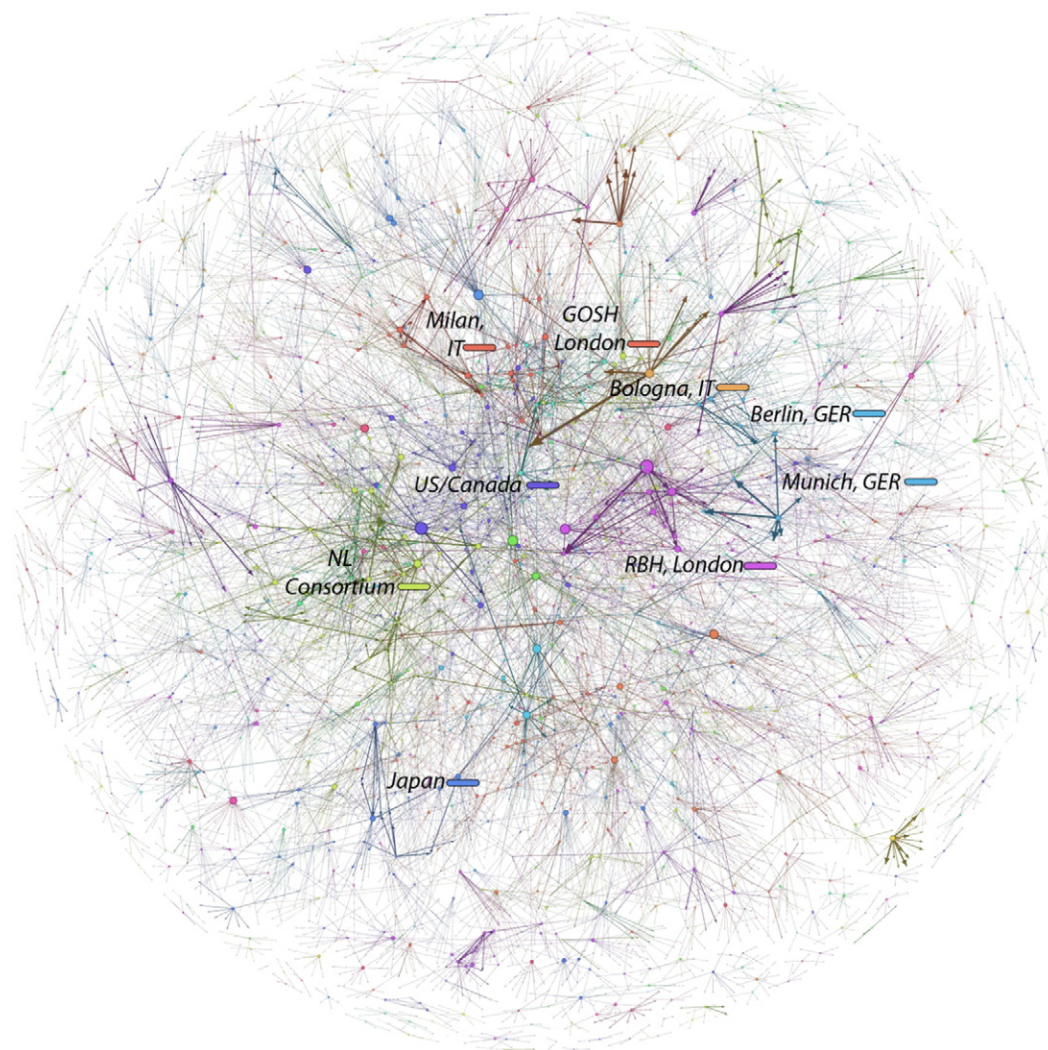


Fig. 5. Network graph (Fruchterman–Reingold representation) of the author-based data set. The size of the nodes corresponds to the out-degree centrality of the node, the weight assigned to the ties corresponds to the cumulative impact factor of the particular link. Node clusters are colored automatically based on modularity. The labels were added manually to highlight some of the visually most prominent nodes and to help the reader to associate (automatically assigned) color codes with concrete institutions. It should be emphasized that not all nodes within a color-area (network cluster) are necessarily from that particular geographic area. GOSH = Great Ormond Street/Heart Hospital, London; RBH = Royal Brompton Hospital, London.

planning. As a consequence a top-down approach may have potentially harmful impact on the system in this setting [28,29]. For example, one of the unintended consequences of centralistic consolidation attempts could lie in the creation of an environment of distrust and competitiveness rather than one of nurturing collaboration. Furthermore, given recent efforts to quantify research output of different institutions based on isolated local metrics of academic output, the current study illustrates some of the dangers of this approach. Inspection of Fig. 5 and the results of the key player analysis show that two of the most prominent nodes on a *global* scale (Royal Brompton Hospital, London and Great Ormond Street/Heart Hospital, London, UK) were recently placed at risk of being afflicted by a uni-national review process aimed at reforming paediatric cardiology centers in England. The current analysis highlights that beyond local human capital and capital assets available, the value of (intangible) social capital accumulated over time must not be ignored. Unlike the two former forms of capital, social capital may be difficult to relocate and the effects of restructuring established structures are difficult to predict and maybe detrimental. On the contrary, the creation of a central national ACHD research infrastructure for ACHD by the profession (with a bottom-up approach) has the potential to improve collaboration and enhance research output. Examples include the Dutch CONCOR Network and the German Competence

Network for Congenital Heart Disease [30,31]. In fact, analyzing the publication records we could show that publications emerging from the latter organization involved a median of 13 institutions. We submit, herewith, that such structures should be encouraged as they create a powerful research infrastructure and act as condensation points for enhancing joint research efforts and output. Furthermore, collaboration is essential for a heterogeneous field such as ACHD so both retrospective and prospective studies are adequately powered.

The current analysis offers insights into the structure of ACHD research beyond identifying major players in the field. Network analysis illustrates the structure of research collaboration and reveals functional units [20] that may not coincide with individual institutions. Rather it may aid to decompose the network into closely connected subunits, characterized by personal links or shared research interests. It is hoped that future projects may uncover the distribution of particular research interests/areas to facilitate the creation of a true innovation community [32], thus involving and harvesting the potential of the large number of active but currently isolated nodes at the periphery of the network (see Fig. 5). The results of the current report are in agreement with those of previous studies in other medical areas, also supporting the impact of collaboration on academic performance and identification of key areas for future research [33–35].

4.1. Limitations

While co-authorship is the most visible and quantifiable measure of scientific collaboration other forms of cooperation exist that have not been included in the current analysis. This includes especially active involvement in the national and international cardiology associations, guideline committees, participation in annual congresses and invited academic contributions, including Editorials and Letters. For most of these characteristics, however, we lacked adequate data. In addition, we chose to focus on original, peer-reviewed publications rather than invited contributions or review papers.

A well-recognized limitation of bibliometric analyses based on authors' names is the ambiguity related to individuals sharing the same surname and initials. While no definitive remedy for this problem exists, all names were checked manually by one of the authors familiar with the field (G-P.D.) and obvious duplications or alternative spelling were all rectified.

5. Conclusions

Using network analysis methods the current study illustrates the complex and global structure of ACHD research. It also suggests that cooperation between research institutions is associated with higher academic output and may – in part – explain why some countries rank higher in the global ranking list of ACHD research than maybe expected based on country size, national wealth and available medical workforce. As a consequence national and international collaboration in ACHD research should be encouraged and the creation of an adequate supporting infrastructure should be strongly supported.

Conflict of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.ijcard.2015.05.116>.

References

- [1] H. Baumgartner, Geriatric congenital heart disease: a new challenge in the care of adults with congenital heart disease? 2014.
- [2] P. Moons, L. Bovijn, W. Budts, A. Belmans, M. Gewillig, Temporal trends in survival to adulthood among patients born with congenital heart disease from 1970 to 1992 in Belgium, *Circulation* 122 (2010) 2264–2272.
- [3] M.E. Brickner, L.D. Hillis, R.A. Lange, Congenital heart disease in adults. First of two parts, *N. Engl. J. Med.* 342 (2000) 256–263.
- [4] H. Baumgartner, P. Bonhoeffer, N.M. De Groot, F. de Haan, J.E. Deanfield, N. Galie, M.A. Gatzoulis, C. Gohlke-Baerwolf, H. Kaemmerer, P. Kilner, F. Meijboom, B.J. Mulder, E. Oechslin, J.M. Oliver, A. Serraf, A. Szatmari, E. Thaulow, P.R. Vouhe, E. Walma, Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of C, Association for European Paediatric C, Guidelines ESCCFP. Esc guidelines for the management of grown-up congenital heart disease (new version 2010), *Eur. Heart J.* 31 (2010) 2915–2957.
- [5] P. Moons, F.J. Meijboom, H. Baumgartner, P.T. Trindade, E. Huyghe, H. Kaemmerer, Disease ESCWGoG-uCH. Structure and activities of adult congenital heart disease programmes in Europe, *Eur. Heart J.* 31 (2010) 1305–1310.
- [6] K. Niwa, J.K. Perloff, G.D. Webb, D. Murphy, R. Liberthson, C.A. Warnes, M.A. Gatzoulis, Survey of specialized tertiary care facilities for adults with congenital heart disease, *Int. J. Cardiol.* 96 (2004) 211–216.
- [7] H. Baumgartner, W. Budts, M. Chessa, J. Deanfield, A. Eicken, J. Holm, L. Iserin, F. Meijboom, J. Stein, A. Szatmari, P.T. Trindade, F. Walker, Working Group on Grown-up Congenital Heart Disease of the European Society of C. Recommendations for organization of care for adults with congenital heart disease and for training in the subspecialty of 'grown-up congenital heart disease' in Europe: a position paper of the working group on grown-up congenital heart disease of the European society of cardiology, *Eur. Heart J.* 35 (2014) 686–690.
- [8] A. Kempny, R. Fernandez-Jimenez, O. Tutarel, K. Dimopoulos, A. Uebing, Y. Shiina, R. Alonso-Gonzalez, W. Li, L. Swan, H. Baumgartner, M.A. Gatzoulis, G.P. Diller, Meeting the challenge: the evolving global landscape of adult congenital heart disease, *Int. J. Cardiol.* 168 (2013) 5182–5189.
- [9] A. Abbasi, L. Hossain, L. Leydesdorff, Betweenness centrality as a driver of preferential attachment in the evolution of research collaboration networks, *J. Inf.* 6 (2012) 403–412.
- [10] U. Brandes, A faster algorithm for betweenness centrality, *J. Math. Sociol.* 25 (2001) 163–177.
- [11] T. Opsahl, F. Agneessens, J. Skvoretz, Node centrality in weighted networks: generalizing degree and shortest paths, *Soc. Networks* 32 (2010) 245–251.
- [12] S.P. Borgatti, The key player problem, *Dynamic Social Network Modeling and Analysis: Workshop Summary and Papers 2003*, p. 241.
- [13] S.P. Borgatti, Identifying sets of key players in a social network, *Comput. Math. Organ. Theory* 12 (2006) 21–34.
- [14] R development core team, R: a language and environment for statistical computing, 2011.
- [15] M. Salter-Townshend, A. White, I. Gollini, T.B. Murphy, Review of statistical network analysis: models, algorithms, and software, *Statistical Analysis and Data Mining: The ASA Data Science Journal*, 5 2012, pp. 243–264.
- [16] Y.T. Mohmand, A. Wang, Complex network analysis of Pakistan railways, *Discret. Dyn. Nat. Soc.* 2014 (2014).
- [17] D.J. Watts, S.H. Strogatz, Collective dynamics of 'small-world' networks, *Nature* 393 (1998) 440–442.
- [18] T. Evans, Complex networks, *Contemp. Phys.* 45 (2004) 455–474.
- [19] A.-L. Barabási, Scale-free networks: a decade and beyond, *Science* 325 (2009) 412.
- [20] V.D. Blondel, J.-L. Guillaume, R. Lambiotte, E. Lefebvre, Fast unfolding of communities in large networks, *J. Stat. Mech. Theory Exp.* 2008 (2008) P10008.
- [21] M. Brautigam, A. Kempny, R. Radke, H. Baumgartner, G.P. Diller, Spatial and temporal overview of research in pediatric and congenital cardiology: trends and global challenges, *Pediatr. Cardiol.* 35 (2014) 1007–1019.
- [22] A.-L. Barabasi, E. Bonabeau, Scale-free networks, *Sci. Am.* 50–59 (2003).
- [23] M.A. Gatzoulis, Adult congenital heart disease: education, education, education, *Nature clinical practice, Cardiovasc. Med.* 3 (2006) 2–3.
- [24] J.K. Perloff, Adults with surgically treated congenital heart disease. Sequelae and residua, *JAMA* 250 (1983) 2033–2036.
- [25] J. Somerville, Congenital heart disease in adults and adolescents, *Br. Heart J.* 56 (1986) 395–397.
- [26] A.L. Barabasi, N. Gulbahce, J. Loscalzo, Network medicine: a network-based approach to human disease. *Nature reviews, Genetics* 12 (2011) 56–68.
- [27] <http://democracy.Leeds.Gov.Uk/documents/s93411/review%20of%20adults%20with%20congenital%20heart%20disease%20-%20engagement%20on%20revised%20proposals%20-%20appendix%201.Pdf>.
- [28] P. Valckeniers, H. Van Brussel, O. Bochmann, B. Saint Germain, C. Zamfirescu, On the design of emergent systems: an investigation of integration and interoperability issues, *Eng. Appl. Artif. Intell.* 16 (2003) 377–393.
- [29] G.P. Diller, A. Kempny, A. Piorkowski, M. Grubler, L. Swan, H. Baumgartner, K. Dimopoulos, M.A. Gatzoulis, Choice and competition between adult congenital heart disease centers: evidence of considerable geographical disparities and association with clinical or academic results, *Circ Cardiovasc. Qual. Outcomes* 7 (2014) 285–291.
- [30] U. Bauer, E. Niggemeyer, P.E. Lange, the competence network for congenital heart defects. Networking instead of isolated efforts for optimized research and care, *Med. Klin.* 101 (2006) 753–758.
- [31] E.T. van der Velde, J.W. Vriend, M.M. Mannens, C.S. Uiterwaal, R. Brand, B.J. Mulder, Concor, an initiative towards a national registry and DNA-bank of patients with congenital heart disease in the Netherlands: rationale, design, and first results, *Eur. J. Epidemiol.* 20 (2005) 549–557.
- [32] G.P. Pisano, R. Verganti, Which kind of collaboration is right for you, *Harv. Bus. Rev.* 86 (2008) 78–86.
- [33] S. Uddin, L. Hossain, K. Rasmussen, Network effects on scientific collaborations, *PLoS One* 8 (2013) e57546.
- [34] Y. Wu, Z. Duan, Social network analysis of international scientific collaboration on psychiatry research, *Int. J. Ment. Heal. Syst.* 9 (2) (2015).
- [35] Y. Wu, Z. Duan, Visualization analysis of author collaborations in schizophrenia research, *BMC Psychiatry* 15 (2015) 27.