International collaboration as a turning point for sudden cardiac arrest prediction and treatment: the PARQ COST Action

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Sudden cardiac arrest (SCA) is the sudden cessation of the heart's pumping activity, most often due to cardiac arrhythmia, and represents the most prevalent cause of death in high-income countries, striking >300 000 persons per year in Europe and the USA each (Empana *et al.*, 2022).

Most SCA events occur in society (out-of-hospital SCA), where life-saving ambulance treatment may take significant time to arrive; accordingly, average survival rates are currently as low as 5–10% (Gräsner *et al.*, 2020). Moreover, SCA typically occurs unexpectedly in persons presumed to be healthy, although timely cardiologist evaluation is associated with higher survival chances after SCA (van Dongen *et al.*, 2021).

Clearly, there is an urgent need for both improvement in the outcome of SCA victims (by improving resuscitation strategies) and for earlier recognition of at-risk individuals that would allow for the timely institution of preventive strategies. Importantly, there are large differences in SCA characteristics and survival chances after SCA between different European regions, partly driven

by disparities in socio-economic position (Bolijn *et al.*, 2021; van Nieuwenhuizen *et al.*, 2023).

To address these unmet needs, the European Union's COST Action CA19137 "PARQ: Sudden cardiac arrest prediction and resuscitation network: Improving the quality of care" (https://www.cost. eu/actions/CA19137/) was conducted in 2020-2024 (Oliva-Teles et al., 2024). The PARQ project aimed to promote research and knowledge on SCA, thereby extending the collaborations and achievements of the PARQ consortium partners, whose founding members first came together in the European Union Horizon 2020 ESCAPE-NET project of 2017-2022 (https://zenodo. org/communities/escapenet/records? q=&l=list&p=1&s=10&sort=newest).

The main objective of the PARQ project was to create a network of researchers in SCA and resuscitation science from across Europe, covering all identified relevant aspects, from clinical studies to preclinical studies and from ethicolegal studies to socio-economic studies. The specific goals of the PARQ project were to obtain a better understanding of the pathobiology of SCA, to improve the prediction of SCA, to improve survival rates after SCA, and to reduce regional differences in all these aspects across Europe. Working groups were established to meet these goals.

The PARQ project was highly successful in reaching these goals, as indicated by the 58 published papers so far (https://parq-cost.eu/publications/). Some significant results of each working group (WG) are summarised in the following.

Warking group 1

Coordination of sample collection and harmonisation of data

One of the main challenges for SCA and resuscitation research is to harmonise data from different cohorts of patients, thereby avoiding the loss of information (Warming et al., 2022).

WG1 of the PARQ project managed to perform this type of action, starting from the database of SCA patients created in the ESCAPE-NET project and expanding it with many other patients and cohorts from European countries; this was essential for the research carried out in WG2 and WG3.

WG1 also covered another critical issue, i.e. the ethicolegal aspects of observational SCA research. The PARQ project proposed a solution to mitigate this issue by combining technical data protection safeguards with appropriate informed consent policies and proportional ethics oversight.

Moreover, it was suggested that 'codes of conduct' be established in interdisciplinary groups and together with patient representatives to ensure the responsible conduct of data research in emergency medicine (Bak *et al.*, 2023).

Working group 2

Coordination of research aimed at the prevention of SCA

WG2 relied on data sharing from Europe's largest registries of out-of-hospital SCA patients: Paris Sudden Death Expertise Center, Amsterdam Resuscitation Studies, Danish Cardiac Arrest Registry, Swedish Register for Cardiopulmonary Resuscitation, and Lombardia Cardiac Arrest Registry (Warming *et al.*, 2022). This gave the unique opportunity to allow a more accurate estimate of SCA incidence than was previously done and to validate the ARIC risk prediction model of SCA, thus creating a European risk prediction model of SCA and sudden cardiac death (Welten *et al.*, 2023).

The work done in this WG made it possible to focus on a very important issue for Europe in these years: the COVID-19 pandemic. A unique analysis of the impact of the COVID-19 pandemic on SCA incidence and resuscitation management in Europe and worldwide was performed; this type of evidence will be essential to increase our preparedness if and when the next pandemic will strike (Baldi *et al.*, 2024).

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Working group 3

Identification of procedural variations in SCA treatment and best practice definition

One of the most important differences in SCA treatment across different European countries concerns the dispatch of first responders (trained laypeople or trained policemen/firefighters who are alerted in case an SCA event occurs in their vicinity in order to perform much-needed resuscitation before ambulance arrival) (Oving *et al.*, 2021).

The PARQ project had the possibility to greatly expand the knowledge about this issue, demonstrating that European regions with dispatched first responders had higher survival rates than regions without (Oving et al., 2021). Researchers participating in the PARQ project also demonstrated that the dispatch of volunteers in SCA is associated with higher survival rates up to one month after SCA. Also, they described the perceived threats and challenges experienced by first responders during their mission for an out-of-hospital SCA (Baldi et al., 2023).

Moreover, many PARQ researchers participated in international guidelines (Zeppenfeld *et al.*, 2022) and consensus and expert opinion, one of these with participants from 13 countries, organised under the auspices of the German Resuscitation Council, to standardise the description of first responder systems (along with smartphone alerting systems, and automated external defibrillator networks) (Müller *et al.*, 2024).

The network created by PARQ, with a network of SCA researchers among 25 European COST countries (including 10 COST Inclusiveness Target Countries, located mostly in Eastern and Southern Europe), will certainly enable further expansion of our knowledge on these topics in the near future.

Working group 2

Capacity building

The main aim of WG4 was to increase collaboration and networks among SCA researchers in Europe. During the PARQ project, 18 additional countries and 72 researchers joined the founding consortium to participate in this project, making it clear how this COST action could represent a turning point in SCA research in Europe.

Moreover, collaboration with other SCA research groups, e.g. the European Resuscitation Council Research NET and the European Union Horizon 2020 PROFID-EHRA project, were strengthened (Böttiger *et al.*, 2021).

Crucially, WG4 laid the groundwork to sustain such collaborations into the future by organising training schools for junior scientists on various aspects of SCA science and allowing exchange programmes for young researchers that have already yielded various joint publications (Smits *et al.*, 2024).

Unmet needs and future solutions

The PARQ project has clearly achieved important results and paved the way for future studies to fill the knowledge gaps that are still present. The PARQ project members identified several key areas where future research may result in significant breakthroughs in the timely recognition of at-risk individuals, prevention of SCA and better treatment of SCA victims. These areas lie beyond the grounds covered by the PARQ project and include:

- utilisation of state-of-the-art methods that have so far been only sparingly used in SCA research, such as artificial intelligence-supported tools used to improve both diagnosis and treatment, and analysis of genetic factors impacting on SCA risk and/or outcome after SCA
- creation of novel treatments and systems of care to improve the chain of survival after SCA
- extension of the research focus to specific groups of individuals who are at particularly elevated risk of suffering SCA (e.g. patients with cardiogenetic diseases), those in whom SCA and its sequelae impose a particularly heavy burden (e.g. children, young adults), and those who are underserved by the present treatments as witnessed by having lower SCA survival chances (e.g. women [Blom et al., 2019], individuals with lower socio-economic position [van Nieuwenhuizen et al., 2019])
- extension of the research focus to long-term limitations and disabilities after SCA (particularly in presently underresearched areas such as psychological, emotional and societal functioning) in order to delineate this problem, identify at-risk or affected individuals and underlying causes, and develop effective preventive and therapeutic strategies
- development of quality indicators of SCA treatment as already developed for SCA prevention (Aktaa et al., 2023).

These key areas may be the basis for future research projects aimed at further reducing the burden that SCA imposes on both individuals and society at large across Europe and beyond. Such future projects should be focused on international collaboration to be truly successful and impactful, as the scientists who collaborated in the PARQ project (and the preceding ESCAPENET project) have demonstrated.

References

Aktaa, S., Tzeis, S., Gale, C.P., Ackerman, M.J., Arbelo, E., Behr, E.R., Crotti, L., d'Avila, A., de Chillou, C., Deneke, T., Figueiredo, M., Friede, T., Leclercq, C., Merino, J.L., Semsarian, C., Verstrael, A., Zeppenfeld, K., Tfelt-Hansen, J. and Reichlin, T. (2023) 'European Society of Cardiology quality indicators for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death', *Europace*, 25, pp. 199–210. doi: 10.1093/europace/euac114.

Bak, M.A.R., Vroonland, J.C.H., Blom, M.T., Damjanovic, D., Willems, D.L., Tan, H.L. and Ploem, M.C. (2023) 'Data-driven sudden cardiac arrest research in Europe: Experts' perspectives on ethical challenges and governance strategies', *Resuscitation Plus*, 15, 100414. doi: 10.1016/j.resplu.2023.100414.

Baldi, E., D'Alto, A., Benvenuti, C., Caputo, M.L., Cresta, R., Cianella, R. and Auricchio, A. (2023) 'Perceived threats and challenges experienced by first responders during their mission for an out-of-hospital cardiac arrest', *Resuscitation Plus*, 14, 100403. doi: 10.1016/j.resplu.2023.100403.

Baldi, E., Klersy, C., Chan, P., Elmer, J., Ball, J., Counts, C.R., Grunau, B., Xie, J., Straney, L., Youngquist, S.T., Bray, J.E., Matsuyama, T. and Nolan, J.P. (2024) 'The impact of COVID-19 pandemic on out-of-hospital cardiac arrest: An individual patient data meta-analysis', *Resuscitation*, 194, 110043. doi: 10.1016/j. resuscitation.2023.110043.

Blom, M.T., Oving, I., Berdowski, J., van Valkengoed, I.G.M., Bardai, A. and Tan, H.L. (2019) 'Women have lower chances than men to be resuscitated and survive out-of-hospital cardiac arrest', *European Heart Journal*, 40, pp. 3842–3834. doi: 10.1093/eurheartj/ehz297.

Bolijn, R., Sieben, C.H.A.M., Kunst, A.E., Blom, M., Tan, H.L. and van Valkengoed, I.G.M. (2021) 'Sex differences in incidence of out-of-hospital cardiac arrest across ethnic and socioeconomic groups: A population-based cohort study in the Netherlands', *International Journal of Cardiology*, 343, pp. 156–161. doi: 10.1016/j.ijcard.2021.09.007.

Böttiger, B.W., Tan, H.L., Semeraro, F., Monsieurs, K.G. and Perkins, G.D. (2021) 'The ERC Research NET — Success, current status and perspectives of the international network for cardiac arrest, resuscitation and post-resuscitation care research', *Resuscitation*, 165, pp. 127–129. doi: 10.1016/j. resuscitation.2021.06.012.

van Dongen, L.H., Blom, M.T., de Haas, S.C.M., van Weert, H.C.P.M., Elders, P.J.M. and Tan, H.L. for the ESCAPE-NET Investigators (2021) 'Higher chances of survival to hospital admission after out-of-hospital cardiac arrest in patients with previously diagnosed heart disease', *Open Heart*, 8, e001805. doi: 10.1136/openhrt-2021-001805.

Empana, J.P., Lerner, I., Valentin, E., Folke, F., Böttiger, B., Gislason, G., Jonsson, M., Ringh, M., Beganton, F., Bougouin, W., Marijon, E., Blom, M., Tan, H. and Jouven, X. (2022) 'Incidence of sudden cardiac death in the European Union', *Journal of the American College of Cardiology*, 79(18), pp. 1818–1827. doi: 10.1016/j. jacc.2022.02.041.

Gräsner, J.T., Wnent, J., Herlitz, J., Perkins, G.D., Lefering, R., Tjelmeland, I.B., Koster, R.W., Masterson, S., Rossell-Ortiz, F., Maurer, H., Strömsöe, A., Burkart, R., Caccioppola, A., Cimpoesu, D., Delassus, P., Hovdenes, J., Ioannides, M., Maconochie, I., Paal, P., Ristagno, G., Skogvoll, E., Smith, G.B., Wissenberg, M. and Böttiger, B.W. (2020) 'Survival after out-of-hospital cardiac arrest in Europe - Results of the EuReCa TWO study', *Resuscitation*, 148, pp. 218–226. doi: 10.1016/j.resuscitation.2019.12.042.

Müller, M.P., Metelmann, C., Thies, K.C., Greif, R., Scquizzato, T., Deakin, C.D., Auricchio, A., Barry, T., Berglund, E., Böttiger, B.W., Burkart, R., Busch, H.J., Caputo, M.L., Cheskes, S., Cresta, R., Damjanovic, D., Degraeuwe, E., Ekkel, M.M., Elschenbroich, D., Fredman, D., Ganter, J., Gregers, M.C.T., Gronewald, J., Hänsel, M., Henriksen, F.L., Herzberg, L., Jonsson, M., Joos, J., Kooy, T.A., Krammel, M., Marks, T., Monsieurs, K., Ng, W.M., Osche, S., Salcido, D.D., Scapigliati, A., Schwietring, J., Semeraro, F., Snobelen, P., Sowa, J., Stieglis, R., Tan, H.L., Trummer, G., Unterrainer, J., Vercammen, S. and Wetsch, W.A. (2024) 'Reporting standard for describing first responder systems, smartphone alerting systems, and AED networks', *Resuscitation*, 195, 110087. doi: 10.1016/j.resuscitation.2023.110087.

Oving, I., de Graaf, C., Masterson, S., Koster, R.W., Zwinderman, A.H., Stieglis, R., AliHodzic, H., Baldi, E., Betz, S., Cimpoesu, D., Folke, F., Rupp, D., Semeraro, F., Truhlar, A., Tan, H.L. and Blom, M.T. (2021) 'European first responder systems and differences in return of spontaneous circulation and survival after out-of-hospital cardiac arrest: A study of registry cohorts', *Lancet Regional Health - Europe*, 1, 100004. doi: 10.1016/j.lanepe.2020.100004.

Oliva-Teles, N., Baldi, E., Böttiger, B.W., Empana, J.P., Jonsson, M., Ristagno, G., Tfelt-Hansen, J. and Tan, H.L. (2024) 'Lifting the burden of sudden cardiac arrest through international collaboration: the PARQ project (EU-COST Action)', *JACC Advances*. In press. doi: 10.1016/j.jacadv.2024.101226.

Smits, R.L.A., Sødergren, S.T.F., Folke, F., Møller, S.G., Ersbøll, A.K., Torp-Pedersen, C., van Valkengoed, I.G.M. and Tan, H.L. (2024) 'Long-term survival following out-of-hospital cardiac arrest in women and men: Influence of comorbidities, social characteristics, and resuscitation characteristics', *Resuscitation*, 201, p. 110265. doi: 10.1016/j.resuscitation.2024.110265.

van Nieuwenhuizen, B.P., Oving, I., Kunst, A.E., Daams, J., Blom, M.T., Tan, H.L. and van Valkengoed, I.G.M. (2019) 'Socio-economic differences in incidence, bystander cardiopulmonary resuscitation and survival from out-of-hospital cardiac arrest: a systematic review', *Resuscitation*, 141, pp. 44–62. doi: 10.1016/j. resuscitation.2019.05.018.

van Nieuwenhuizen, B.P., Tan, H.L., Blom, M.T., Kunst, A.E. and van Valkengoed, I.G.M. (2023) 'Association between income and risk of out-of-hospital cardiac arrest: a retrospective cohort study', *Circulation: Cardiovascular Quality and Outcomes*, 16(2), e009080. doi: 10.1161/CIRCOUTCOMES.122.009080.

Warming, P.E., Ågesen, F.N., Lynge, T.H., Jabbari, R., Smits, R.L.A., van Valkengoed, I.G.M., Welten, S.J.G.C., van der Heijden, A.A., Elders, P.J., Blom, M.T., Jouven, X., Schwartz, P.J., Albert, C.M., Beulens, J.W., Rutters, F., Tan, H.L., Empana, J.-P. and Tfelt-Hansen, J. (2022) 'Harmonization of the definition of sudden cardiac death in longitudinal cohorts of the European Sudden Cardiac Arrest network – towards Prevention, Education, and New Effective Treatments (ESCAPE-NET) consortium', American Heart Journal, 245, pp. 117–125. doi: 10.1016/j.ahj.2021.12.008.

Welten, S.J.G.C., Remmelzwaal, S., Blom, M.T., van der Heijden, A.A., Nijpels, G., Tan, H.L., van Valkengoed, I., Empana, J.P., Jouven, X., Ågesen, F.N., Warming, P.E., Tfelt-Hansen, J., Prescott, E., Jabbari, R. and Elders, P.J.M. (2023) 'Validation of the ARIC prediction model for sudden cardiac death in the European population: The ESCAPE-NET project', *American Heart Journal*, 262, pp. 55–65. doi: 10.1016/j. ahj.2023.03.018.

Zeppenfeld, K., Tfelt-Hansen, J., de Riva, M., Winkel, B.G., Behr, E.R., Blom, N.A., Charron, P., Corrado, D., Dagres, N., de Chillou, C., Eckardt, L., Friede, T., Haugaa, K.H., Hocini, M., Lambiase, P.D., Marijon, E., Merino, J.L., Peichl, P., Priori, S.G., Reichlin, T., Schulz-Menger, J., Sticherling, C., Tzeis, S., Verstrael, A., Volterrani, M. and ESC Scientific Document Group (2022) '2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death', *European Heart Journal*, 43(40), pp. 3997–4126. doi: 10.1093/eurheartj/ehac262.



PROJECT SUMMARY

PARQ aims to create a network of researchers across Europe whose overall aim is to reduce the societal burden of sudden cardiac arrest (SCA). To reach this aim, PARQ will conduct studies that focus on two dimensions: (1) prevention of SCA through the discovery of its inherited, acquired, and environmental causes, and their interaction, and improved recognition of individuals at risk; and (2) improvement of survival chances after SCA through the development and implementation of resuscitation treatments in the community.

PROJECT PARTNERS

At present, the PARQ consortium consists of partners from 25 COST countries across Europe: Austria, Belgium, Bosnia Herzegovina, Cyprus, Denmark, Estonia, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Malta, Netherlands, North Macedonia, Norway, Portugal, Romania, Slovakia, Spain, Sweden, Switzerland, Turkey and the United Kingdom

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