

Forschungsaktivitäten 2021 – Research Report 2021

**Departement für Intensivmedizin und Neonatologie
Universitäts-Kinderspital Zürich**

**Department of Intensive Care and Neonatology,
University Children's Hospital Zurich**



Table of Contents

I.	INTRODUCTION & SUMMARY	3
II.	ORIGINAL ARTICLES	5
III.	ACCEPTED PUBLICATIONS (in press or published early 2022)	11
IV.	REVIEWS	13
V.	LETTERS TO THE EDITOR AND CASE REPORTS	13
VI.	BOOK CHAPTERS	13
VII.	GRADUATIONS	14
VIII.	SUPERVISION OF PhD STUDENTS	14
IX.	MEDICAL DOCTORAL THESIS AND MASTER THESIS (completed in 2021)	15
X.	RECEIVED GRANTS AS CHIEF INVESTIGATOR	15
XI.	INVITED KEYNOTE PRESENTATIONS	16
XII.	ORAL PRESENTATIONS	19
XIII.	POSTER PRESENTATIONS	20
XIV.	MEDIA ACTIVITIES	20

I. INTRODUCTION & SUMMARY

Dear colleagues,

It is with great pleasure that we hereby present the report on 2021 research activities by the PINNACLE research group of the Department of Intensive Care and Neonatology at University Children's Hospital, and at the Children's Research Center.

PINNACLE stands for Pediatric and Neonatal Intensive Care Research Group and was formed at the beginning of 2021 to unite and cross-fertilize the highly interdisciplinary research working a focus on critically ill children and neonates at the University Children's Hospital Zürich. The word "pinnacle" refers to a peak or mountain summit. PINNACLE thereby not only represents the characteristic Swiss landscape; in addition, some of our patient families describe the experience of intensive care as "climbing a mountain". We see therefore "pinnacle" as a metaphor of challenges, aspirations, and achievements forming the core of our research group. Our overall aim is to embed research as a standard of care in neonatal and pediatric intensive care, enabling innovation and quality improvement leading to better short- and long-term outcomes for our patients.

The 2021 PINNACLE Research report demonstrates the diversity of the group spanning from basic science, healthcare quality and outcome research, to interventional trials. The over 70 publications highlight the activity at local, national, and international level, with partnerships with worldwide leading institutions such as Imperial College. Moreover, particular attention is given to the promotion of young researchers, who successfully contributed with several publications.

Several grants including SNF and NIH help to set the basis to further expand that work over coming years. Two important milestones for the future will be to further implement the interdisciplinary work by supporting novice and early career researchers from medical, nursing, allied health, and other disciplines. Second, particular attention will be given to the development of an active partnership work with patients, families, and public during all stages of the research process (patient and parent involvement – PPI).

In this dynamic research environment, we are particularly grateful to have been able to employ a core study coordinator team at the end of 2021. The recruitment of Elisa Zimmermann, Kathrin Weber, and Marion Meier enhances our research capacity and brings unique expertise to the team to conduct trials, as evidenced by the successful conduction of the SwissPed Recovery RCT on children with COVID-19 associated Paediatric Inflammatory Multisystem Syndrome, and several other studies underway. Furthermore, we are most thankful for the strong support from the Children's Research Center (CRC) which has been essential to enhance the research capacity of our department.

Finally, we would like to thank all PINNACLE team members, the staff of the Department of Intensive Care and Neonatology, our partners, and the Children's Research Center at University Children's Hospital Zürich for their activities and support for research as a key part of high quality care.

Most importantly, we are grateful for the willingness of families to participate in research during challenging and stressful times, hoping to help improving outcomes for children in the future.

Your

C. Hagmann *Luregn Schlapbach*

Cornelia Hagmann and Luregn Schlapbach



Picture from the 2022 Start of the Year PINNACLE Research Group meeting
(note: not all members present on the picture)

II. ORIGINAL ARTICLES

1. Adams, M., **Brotschi, B.**, Birkenmaier, A., Schwendener, K., Rathke, V., Kleber, M., **Hagmann, C.**, and Swiss National Asphyxia Cooling Register Group, *Process variations between Swiss units treating neonates with hypoxic-ischemic encephalopathy and their effect on short-term outcome.* J Perinatol, 2021. 41(12): p. 2804-2812.
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38. Scheidegger, S., Held, U., **Grass, B.**, Latal, B., **Hagmann, C.**, **Brotschi, B.**, on behalf of the National Asphyxia and Cooling Register Group, *Association of perinatal risk factors with neurological outcome in neonates with hypoxic ischemic encephalopathy*. *J Matern Fetal Neonatal Med*, 2021. 34(7): p. 1020-1027.
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45. Simpson, A., Long, D., Fleischmann-Struzek, C., Minogue, J., Venkatesh, B., Hammond, N.E., Tian, D.H., and **Schlapbach, L.J.**, *Long-Term Functional Outcomes After Sepsis for Adult and Pediatric Critical Care Patients-Protocol for a Systematic Review.* Front Pediatr, 2021. 9: p. 734205.
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48. Tai, C.W., Gibbons, K., Schibler, A., **Schlapbach, L.J.**, and Raman, S., *Acute kidney injury: epidemiology and course in critically ill children.* J Nephrol, 2021. DOI: 10.1007/s40620-021-01071-5
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III. ACCEPTED PUBLICATIONS (in press or published early 2022)

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2. **Baumann, P.**, Greco, F., L'Abate, P., Wellmann, S., Wiegert, S., and Cannizzaro, V., *Lung-borne systemic inflammation in mechanically ventilated infant rats due to high PEEP, oxygen, and hypoxemia*. *Am J Transl Res*, 2022. 14(1): p. 343-354.
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5. Doo, I., Staub, L.P., Mattke, A., Haisz, E., Seidler, A.L., Alphonso, N., and **Schlapbach, L.J.**, *Diagnostic Accuracy of Infection Markers to Diagnose Infections in Neonates and Children Receiving Extracorporeal Membrane Oxygenation*. Frontiers in Pediatrics, 2022. In Press.
6. Menon, K., **Schlapbach, L.J.**, Akech, S., Argent, A., Biban, P., Carrol, E.D., Chiotos, K., Jobayer Chisti, M., Evans, I.V.R., Inwald, D.P., Ishimine, P., Kissoon, N., Lodha, R., Nadel, S., Oliveira, C.F., Peters, M., Sadeghirad, B., Scott, H.F., de Souza, D.C., Tissieres, P., Watson, R.S., Wiens, M.O., Wynn, J.L., Zimmerman, J.J., Sorce, L.R., *Criteria for Pediatric Sepsis-A Systematic Review and Meta-Analysis by the Pediatric Sepsis Definition Taskforce*. Crit Care Med, 2022. 50(1): p. 21-36.
7. **Schlapbach, L.J.** and Coin, L., *Understanding Detrimental Host Response to Infection-The Promise of Transcriptomics*. Pediatr Crit Care Med, 2022. 23(2): p. 133-135.
8. **Schlapbach, L.J.**, Weiss, S.L., Bembea, M.M., Carcillo, J., Leclerc, F., Leteurtre, S., Tissieres, P., Wynn, J.L., Zimmerman, J.J., Lacroix, J., on behalf of the Pediatric Organ Dysfunction Information Update Mandate (PODIUM) Group, *Comparison of Scoring Systems for Organ Dysfunction and Multiple Organ Dysfunction*. Pediatrics, 2022. In Press.
9. Weiss, S.L., Carcillo, J., Leclerc, F., Leteurtre, S., **Schlapbach, L.J.**, Tissieres, P., Wynn, J.L., Lacroix, J., on behalf of the Pediatric Organ Dysfunction Information Update Mandate (PODIUM) Group, *The Case for a "Syndrome" of Pediatric MODS*. Pediatrics, 2022. In Press.
10. Tomaszewski, W., Ablaza, C., Straney, L., Taylor, C., Millar, J., **Schlapbach, L.J.**, *Educational Outcomes of Childhood Survivors of Critical Illness-A Population-Based Linkage Study*. Crit Care Med, 2022. In Press.

IV. REVIEWS

1. Harley, A., **Schlapbach, L.J.**, Johnston, A.N.B., and Massey, D., *Challenges in the recognition and management of paediatric sepsis - The journey*. Australas Emerg Care, 2021. DOI: 10.1016/j.auec.2021.03.006
2. Hayes, R., Hartnett, J., Semova, G., Murray, C., Murphy, K., Carroll, L., Plapp, H., Hession, L., O'Toole, J., McCollum, D., Roche, E., Jenkins, E., Mockler, D., Hurley, T., McGovern, M., Allen, J., Meehan, J., Plotz, F.B., Strunk, T., de Boode, W.P., Polin, R., Wynn, J.L., Degtyareva, M., Kuster, H., Janota, J., Giannoni, E., **Schlapbach, L.J.**, Keij, F.M., Reiss, I.K.M., Bliss, J., Koenig, J.M., Turner, M.A., Gale, C., Molloy, E.J., *Neonatal sepsis definitions from randomised clinical trials*. *Pediatr Res*, 2021. DOI: 10.1038/s41390-021-01749-3
3. **Schlapbach, L.J.**, de Oliveira, C.F., Raman, S., and de Souza, D., *Metabolic resuscitation in pediatric sepsis: a narrative review*. *Transl Pediatr*, 2021. 10(10): p. 2678-2688.

V. LETTERS TO THE EDITOR AND CASE REPORTS:

1. Long, E., **Schlapbach, L.J.**, and Babl, F.E., *The challenge of infrequency*. *Acta Paediatr*, 2021. 110(3): p. 1075.

VI. BOOK CHAPTERS

1. **Burren, J.**, *Handbook of Paediatric and Neonatal Mechanical Ventilation*. 2021. Second Edition. ISBN: 978-84-124534-0-9
2. Giannoni, E. and **Schlapbach, L.J.**, *Editorial: Sepsis in Neonates and Children*. *Front Pediatr*, 2020. 8: p. 621663.
3. Schiestl, C., Meuli, M., Vojvodic, M., Pontiggia, L., Neuhaus, D., **Brotschi, B.**, Reichmann, E., Böttcher-Haberzeth, S., and Neuhaus, K., *Expanding into the future: First time combination of a novel dermal template and distinct variants of autologous cultured skin substitutes for massive burns*. *Burns Open*, Elsevier, 2021. 5(3).
4. Scholefield, B.C., Reiter, K.D.C., Agrawal, S., Amigoni, A., Castelão, M., Iodice, F., Ntouzepi, K., Schettler, K.F., Ilia, S., Torres, E., Tziouvas, K., Zoica, B., **Zivkovic, V.**, and Pappachan, J., *Update in Paediatric and Neonatal Intensive Care 2021*. *Neurocritical care 2021 ESPNIC*, 2021.

VII. GRADUATIONS

Prof. Dr. med. Cornelia Hagmann: Titularprofessur, University of Zurich 2021

PD Dr. med. Beate Grass: Habilitation, University of Zurich 2021

VIII. SUPERVISION OF PhD STUDENTS

L. Schlapbach

- **since 2019**
 - PhD Supervisor of Amanda Harley: "Paediatric Sepsis", the University of Queensland
 - PhD Supervisor of Michelle Cree: "Pharmacokinetics on ECMO", the University of Queensland
- **since 2020**
 - PhD Supervisor of Quyen Hu – Automatic dosing software in critically ill children, the University of Queensland
- **since 2021**
 - Honorary Supervision of Zoe Sever – Parental concern in sepsis, the University of Queensland

L. Schlapbach und E. Kühlwein

- **since 2021**
 - PhD Supervisor of Larissa Bürki: "Nutritional Programme Implementation", the University of Vienna

C. Hagmann

- **since 2020**
 - PhD Supervisor of Alexandra Stöckli: "Executive function profile of children born pre-term and children born with congenital heart disease", Clinical Science PhD Programme, UZH

IX. MEDICAL DOCTORAL THESIS AND MASTER THESIS (completed in 2021)

B. Brotschi

- Doctoral thesis, Simone Scheidegger: "Association of perinatal risk factors with neurological outcome in neonates with hypoxic ischemic encephalopathy" (faculty of medicine, University of Zurich)

C. Hagmann

- Doctoral thesis, Mirjam Hug: "Brain volumes and neurological developmental outcome at the corrected age of two years in premature infants: an observational study" (faculty of medicine, University of Zurich)
- Master thesis, Fiona Balsiger: „Der sonderpädagogische Förderbedarf von Kindern, die sehr oder extrem frühgeboren wurden, im Vergleich zu termingeborenen Kindern“ (faculty of medicine, University of Zurich)
- Master thesis, Tina Mauthe: „Auswertung des Elternbild-Fragebogens für Kinder und Jugendliche im Rahmen der EpoKids Studie und Vergleich der Eltern-Kind-Beziehungsqualität von termingeborenen oder frühgeborenen Kindern“ (faculty of medicine, University of Zurich)

B. Frey

- Doctoral thesis, Romana Salvini: "Iatrogenic events contributing to paediatric intensive care unit Admission" (faculty of medicine, University of Zurich)

X. RECEIVED GRANTS AS CHIEF INVESTIGATOR

L. Schlapbach

- 2021 RECOVERY PIMS study (CIA). Gaydoul foundation 50'000 CHF
- 2021 RECOVERY PIMS study (CIA). Vontobel foundation 120'000 CHF
- 2021 RECOVERY PIMS study (CIA). Nomis foundation 270'000 CHF
- 2021 RECOVERY PIMS basic science study (CIA) Nomis foundation 200'000 CHF
- 2021 Machine Learning in the Swiss Pediatric Sepsis Study (CIA). Swiss National Science Foundation 930'302 CHF
- 2021 Pediatric Sepsis Criteria and Clinical Decision Support Tools. National Institute of Health (PI) 3'044'659 USD

- 2021 Machine learning for precision medicine in paediatric critical care. Ramaciotti Foundation (CIC) 99'733 AUD
- 2021 Commercialisable Aptamer-based Diagnostics for Sepsis Point of Care. NHMRC (Associate Investigator) 1,043'143 AUD

C. Hagmann

- 2021 RCT Kreative Musiktherapie bei CHD. Refugium Foundation 10'000 CHF
- 2021 RCT Kreative Musiktherapie bei CHD. Kinder Herz Stiftung 10'000 CHF
- 2021 RCT Kreative Musiktherapie bei CHD. Marta Maria von Schlitz 56'538 CHF
- 2021 „Profile der exekutiven Funktionen und strukturellen Hirnkonnektivität in Kinder mit Risiken für Entwicklungsbeeinträchtigungen“ Anna Müller-Grocholski foundation CHF113'367

B. Grass

- 2021 Filling the Gap, University of Zurich, salary for 30% protected research time

U. Kennedy

- 2021 Gender and sepsis in children, FZK 60'000 CHF

XI. INVITED KEYNOTE PRESENTATIONS

L. Schlapbach

- *The Graduate – long-term outcomes after ICU, Paediatric Study Group Update*
ANZICS CTG Annual Meeting, March 2021
- *Paediatric Inflammatory Multisystem Syndrome*
6th PIGS course, Bern, March 2021
- *ECMO in pediatric sepsis*
EuroELSO Virtual Congress, May 2021
- *What is dysregulated host response in children? Is it sepsis? The search for the holy grail*
International Sepsis Forum, Sao Paulo, Brazil, May 2021
- *Simple is beautiful: the future of intensive care? The next generation of feedback circuits. Quality and safety in the next decade, beyond reliability*
National Congress of Critical Care Medicine, Colombia, AMCI, May 2021

- *We really need a new pediatric sepsis definition. Hydrocortisone, vitamins & Co – just another magic bullet missing the target?*
ESPIC Virtual Congress, June 2021
- *Paediatric COVID experience – ANZ and abroad*
CICM ASM 2021, July 2021
- *MIS-C*
31st ECCMID conference, June 2021
- *Sepsis now and into the future: Sepsis protocols*
Asia Pacific Intensive Care Symposium (APICS), July 2021
- *New paediatric sepsis guidelines: What's new?*
Swiss Society of Intensive Care Congress, September 2021
- *HLH and sepsis: similar but not the same*
1st European Paediatric Onco-Critical Care symposium, September 2021
- *New Pediatric Sepsis Guidelines: What's New?*
Swiss Society of Intensive Care, Interlaken, September 2021
- *Organ Donation in Pediatrics*
4th UEMS/BTC course for transplant coordinators, September 2021
- *PIMS-TS*
Armenian Pediatric Association, October 2021
- *Update on PIMS-TS*
Swiss Pediatric Refresher, October 2021

C. Hagmann

- *Music intervention in NICU*
GNPI 2021, June 2021
- *Sounding Together: Creative Music Therapy for preterm infants Music*
Development and Rehabilitation in Geneva July 2021

B. Grass

- *Herausforderung bei Notfällen im Säuglingsalter*
KNiRPS Kongress 2021

L. Bürki

- *Ernährungstherapie in der pädiatrischen Intensivmedizin*
Master of Science Studiengang Ernährung und Diätetik an der BFH July 2021

XII. ORAL PRESENTATIONS

B. Brotschi

- "PREPICare: An intelligent, pressure distributing positioning system for critically ill neonates in paediatric intensive care: First insights from a pilot study. Annual Meeting of the Swiss Society of intensive Care, 2021
- Workshop: Target Temperature Management: Stolpersteine bei pädiatrischen Patienten. Annual Meeting of the Swiss Society of intensive Care, 2021
- Peripartale Asphyxie in der Schweiz. Zentralschweizer Symposium Pediatric Care 2021
- Einbezug der Angehörigen für Therapieentscheid. Netzwerksymposium Donor Care Association 2021
- Target Temperature Management: Stolpersteine bei pädiatrischen Patienten. Annual Meeting of the Swiss Society of intensive Care, 2021

B. Grass

- Training ICU staff for neonatal transport – the Swiss experience ESPNIC, Athens, Greece 2021

V. Zivkovic (Vortragende) und Barbara Brotschi, Janet Kelly, Kevin Schmid, Eva Kühlwein

- Pathologic fractures in pediatric intensive care patients – an underestimated complication of chronic critically ill children; two case reports and a literature review, Annual Meeting of the Swiss Society of intensive Care, 2021

B. Frey und R. Salvini

- Iatrogenic events contributing to paediatric intensive care unit admission. Annual Meeting of the Swiss Society of intensive Care, 2021

Y. Kröger und J. Henkel

- Emergence Delir, Swiss Society of intensive Care Conference 2021

J. Henkel

- Chylothorax IG für angeborene Herzfehler 2021

XIII. POSTER PRESENTATIONS

B. Brotschi

- From Influenza A to cardiac arrest in two days. Swiss Society of Pediatric Conference, June 2021

V. Zivkovic

- Pathologic fractures in pediatric intensive care patients – an underestimated complication of chronic critically ill children; two case reports and a literature review. Swiss Society of intensive Care Conference, September 2021

N. Abadir

- Challenging airway management in congenital syngnathia. Swiss Society of intensive Care Conference, September 2021

Y. Kröger

- Zwischen Himmel und Hölle – eine qualitative Studie zu den Erfahrungen von Eltern mit einem kritisch kranken Kind mit extrakorporaler Membranoxygenierung . Swiss Society of intensive Care Conference, September 2021

A. Jakob / S. Naji

- Routinemässiges Anspülen bei endotrachealem Absaugen ja/nein? Swiss Society of intensive Care Conference, September 2021

XIV. MEDIA ACTIVITIES

L. Schlapbach:

- **Covid-19 Wenn Kinder schwerst erkranken**, Podcast med Audio Feb 21
<https://medical-tribune.ch/10070227/2021/covid-19-wenn-kinder-schwerst-erkranken>
- **Queensland an international role model for sepsis** | Queensland Health Feb 21
<https://clinicaexcellence.qld.gov.au/about-us/news/queensland-international-role-model-sepsis>

- **Kinderintensivstationen: Coronavirus und PIMS Interview** Feb 2021
<https://vimeo.com/509812752>
- **Artikel/Interview Watson** Jan 2021
<https://www.watson.ch/schweiz/wissen/757130367-pims-corona-effekt-bei-kindern-und-was-du-darueber-wissen-musst>
- **Artikel/Interview NZZ** 2021
<https://nzzas.nzz.ch/wissen/ungeschuetzt-in-den-corona-herbst-die-impfung-fuer-kinder-kommt-wohl-nicht-vor-2022-ld.1644940>
- **Artikel/Interview NZZ** 2021
<https://nzzas.nzz.ch/wissen/ab-herbst-sind-kinder-und-jugendliche-an-der-reihe-was-ihnen-die-corona-impfung-bringt-ld.1607627>