



Naevus
INTERNATIONAL

Annual Newsletter

2019-20

Clinicians Report

Written by Dr Harper Price (Leader of NI Clinicians' Network)

Below are highlight from the clinical CMN literature in 2019.

1: Neuhaus K, Landolt MA, Theiler M, Schiestl C, Masnari O. Skin-related quality of life in children and adolescents with congenital melanocytic nevi – analysis of self- and parent reports. *J Eur Acad Dermatol Venereol*. 2019. A web-based worldwide survey was used to collect data on quality life (QOL) and predictors of impaired QOL with the help of patient advocacy groups. 135 proxy-reported and 28 adolescent reported responses were collected. Most CMN has a moderate effect on QOL, but responses varied, especially in the adolescent group, experiencing a moderate to large impact on QOL. Predictors included older age, visibility of CMN and melanoma.

2: Mosa A, Ho ES, Heinelt M, Wong K, Neuhaus K. Management of congenital melanocytic nevi in the plastic surgery clinic: Families' expectations and their persistent concern about malignancy. *Pediatr Dermatol*. 2019 Nov;36(6):876-881. This group hypothesized that the fear of malignancy is still a common driver to seek surgical removal of CMN in most families. The study was designed as a quality improvement project in 2016 to evaluate the expectations of pediatric patients and their families referred to the plastic surgery clinic at Hospital for Sick Children for CMN management. A two-part anonymous questionnaire before and after initial clinic visit was used to evaluate patient/family concerns. 30 questionnaires were completed (most by mothers) with a patient mean age of 9.2 y (1-25y). Most CMN were small or medium, 1 large; 9 visible when dressed. Results: Referring docs (derms) were rarely concerned about malignancy (8%). Parents listed malignancy as top reason for requesting removal (37%) and expectation for visit, followed by surgical options and outcome. Prior to the clinic visit, 93% were at least slightly worried about CMN growth; 96% worried about malignancy. After the clinic, 63% were at least slightly worried about CMN growth; 72% worried about malignancy.

3: Ben-Ari A, Margalit D, Nachshoni L, Benarroch F. Traumatic Stress Among Children After Surgical Intervention for Congenital Melanocytic Nevi: A Pilot Study. *Dermatol Surg*. 2019 Dec. These authors aim to assess Traumatic Stress Symptoms (PTSS) in children undergoing surgery for CMN through consecutive hospitalizations. Thirty children were voluntarily enrolled prospectively, and children/parents were assessed 4 months after surgical intervention via specific validated assessment tools. After 4 months, children displayed an increase in distress level over baseline, and 33% met criteria for PTSD. Predicting factors included number of procedures, family resources and parental distress, with the latter being most significant.

4: Masnari O, Neuhaus K, Aegerter T, Reynolds S, Schiestl CM, Landolt MA. Predictors of Health-related Quality of Life and Psychological Adjustment in Children and Adolescents With Congenital Melanocytic Nevi: Analysis of Parent Reports. *J Pediatr Psychol*. 2019 Jul 1;44(6):714-725. A cross-sectional study that assessed health-related QOL and psychological adjustment in 235 children ages 1 month to 18 years (avg= 6.3 y) via a web-based survey, parent reported, open over 12 months. Several measures were taken including *Pediatric QOL Inventory 4.0* and *Strengths and Difficulties Questionnaire* and compared to normative data, surgical history, BSA (location, extent and visibility), health status, skin-related discomfort (pain, itch, dry skin, bleeding), *Perceived Stigmatization Questionnaire*, and Socioeconomic status. Parents reported lower HRQOL and higher emotional, behavioral problems in their children/adolescents with CMN, compared to community norms. Impairment predictors were lower SES, neurological problems, skin-related discomfort, perceived stigmatization. Interestingly, overall size of CMN, age/gender, extent of CMN, and removal were not significant predictors. The visibility of skin lesion and psychological adjustment/psychosocial health were found to be mediated by perceived stigmatization.

5: Schaff LR, Marghoob A, Rosenblum MK, Meyer R, Khakoo Y. Malignant transformation of neurocutaneous melanosis (NCM) following immunosuppression. *Pediatr Dermatol*. 2019 Jul;36(4):497-500. This is a case report of a 16-year-old boy with large CMN with multiple satellites and asymptomatic leptomeningeal melanosis who developed melanoma after TNF inhibition (adalimumab X 1, then infliximab) and prednisone for inflammatory bowel disease. Presenting symptoms included intractable headache, photophobia, nausea/vomiting, worse at night, neck/back pain, numbness in leg, double vision and tinnitus. Subsequent CT, lumbar puncture and MRI revealed melanomatous deposits in spine. A VP shunt was placed but the patient passed away 12 weeks after onset of symptoms.



- Children/adolescents with neurological problems, skin-related discomfort, & high levels of perceived stigmatization are vulnerable and may have more impaired QOL and maladjustment. **Special monitoring and supportive services may be needed!**
- Families desire surgical information AND are highly concerned about malignancy.
- There is still misinformation or misconception about melanoma risk.
- Health care providers should provide reliable, easily understandable and coherent information about melanoma risk in CMN and support family decision-making and offer reliable information on indications for surgery and expected outcomes.
- When immunosuppressive therapies are considered for comorbid conditions, both the CMN patient and physician need to consider potential implications for overall melanoma risk.
- Repeated surgical procedures in the hospital may lead to post-traumatic stress symptoms in children with CMN.

Scientific Advancements Report

Written by Dr Maanasa Polubothu (Members of NI Scientific Network)

2019 clinical advances in CMN

Recent important clinical studies/reports:

1) Quality of life and psychologic adjustment predictors

- **Question:** Are there any differences in health-related quality of life (HRQOL) or psychological adjustment in children with CMN versus children without CMN?
- **Methods:** International web-based survey conducted for 12 months, 235 patients completing questionnaires relating to quality of life, strengths and difficulties and perceived stigmatisation
- **Conclusions:** Reported lower HRQOL, higher emotional/behavioral problems in their children/adolescents with CMN, compared to community norms. Predictors for this include: lower socioeconomic status, neurological problems, skin-related discomfort and perceived stigmatization. There is a need for early identification and intervention with psychological support for this group.

2) Management of CMN in the plastic surgery clinic: family expectations and concerns

- **Question:** What information/expectations do patients/carers have about CMN when they attend surgical clinic?
- **Methods:** Two-part anonymous questionnaire before and after initial clinic visit to evaluate patient and family concerns before and after
- **Conclusions:** Families want surgical information and there is misinformation about melanoma risk in families. Better dissemination of accurate information to support families early on to make informed decisions is needed.

3) Final colour of CMN

- **Question:** What is the natural history of spontaneous lightening in CMN?
- **Methods:** Objective measurement of the colour of the CMN and the unaffected skin over time in 110 children
- **Conclusions:** Final CMN colour is related to background pigmentary phenotype, not colour at birth, and is not affected by superficial removal techniques

4) Biker glove pattern of CMN

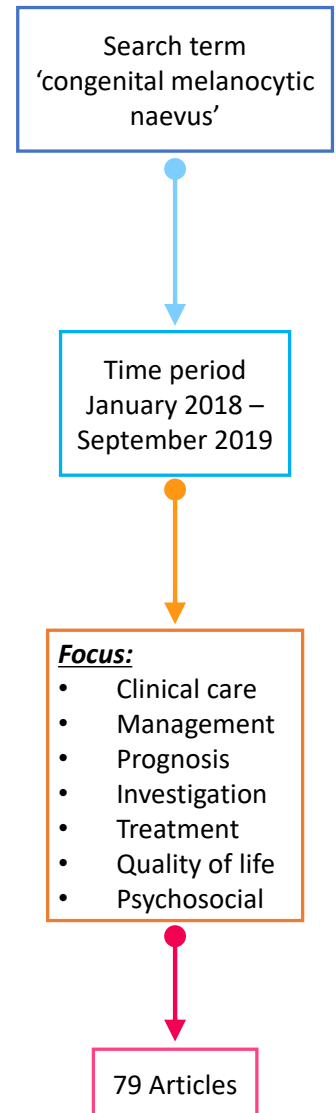
- **Conclusions:** Important for understanding origin and migration patterns of melanocytes; supports hypothesis of Kinsler-Larue melanocyte/naevus cell

5) CMN treated with Trametinib

- **Case:** AKAP9-BRAF fusion CMN with intractable itch treated with MEK inhibitor trametinib
- **Conclusions:** Only a single case but suggests this genetic subgroup may respond to treatment with MEK inhibition



Literature search:



September 2019

Case: Three cases of “biker glove” pattern of CMN (hand/foot CMN with sparing of distal tips and sharp cut off)

Written by:

Dr Maanasa Polubothu
Great Ormond Street Children's hospital
London, UK
with Dr Harper Price
Phoenix Children's Hospital
Phoenix, Arizona

Psychosocial Report

Written by Dr Beatrice de Reviers (Leader of NI Psychosocial Network)

Article : Predictors of Health-related Quality of Life and Psychological Adjustment in Children and Adolescents With Congenital Melanocytic Nevi: Analysis of Parent Reports Ornella Masnari,¹ PHD, Kathrin Neuhaus,² MD, Tilla Aegerter,³ MSC, Shawn Reynolds,⁴ PHD, Clemens M. Schiestl,² MD, and Markus A. Landolt,^{1,3} PHD *Journal of Pediatric Psychology*, 2019, 1–12

Parents of children and adolescents born with NMC significantly reported a lower quality of life, emotional and behavioral problems that were somewhat more important compared to a normal population. Quality of life challenges and psychological adjustment were predicted by lower socioeconomic status, neurological problems, skin-related discomfort (e.g., itching or pain), and the perception of a stigmatization stigma. The size of the NMC and whether the NMC was (partially) suppressed by surgery were not significant predictors.

On the other hand, the visibility factor of the injury has no direct effect on the quality of life of patients as shown by many previous studies on the other hand it has an indirect impact by the perceived stigmatization factor which is then reinforced by this visibility.

Ongoing study by a team of INFOCOM Dijon researchers on the use of one's image when carrying a CMN on social networks and a study on the influencers with CMN, their messages and their scope. Study emulated by association ANNA.

A patient therapeutic education program developed by the ANNA Association and the ANDDI-RARES rare disease health chain, which brought together health professionals and patient associations.

This program applies to children with CMN

Program: E... change your look!

Public: The program is aimed at children aged 6-11 but child-class subgroups: a group of 6-8 years and a group 9-11 years.
Groups of 4 to 8 children

The program is divided into 4 workshops after taking an educational assessment of the child:

Workshop 1: Important concepts to ask.

- understand the differences and similarities between all individuals,
- understand natural curiosity to accept to guide it with kindness.
- take stock of the child's medical knowledge of the origin of the child's difference.

Workshop 2: Introduce yourself and respond to curiosity

- How to introduce myself and prepare for anxious situations
- How to respond to curiosity about my physical peculiarity

This workshop aims to personalize each child's responses so that they can take ownership of them by experimenting with them.

Workshop 3: Emotions

- Understand my emotions and therefore the reactions they induce
- Understanding the emotions of others and therefore their reactions

Workshop 4: Confronting others and delicate situations.

With the three previous workshops, the child will be able to face difficult situations that he has chosen to work on.

Last time: Individual evaluation of the program with each child based on the travel diary and in particular the last pages of this booklet.

The program draws on children's imaginations and takes them on a hot air balloon trip, each stop of which corresponds to one stage of the program. A travel diary will follow the child throughout his adventures. He will be accompanied in his quest by the pilot of the hot air balloon who will play the role of a guide.

An accompanying briefcase for the program. It contains all the tools necessary to facilitate these workshops (travel diary, flight plan, Checklist, Passport, boarding card, situation maps).

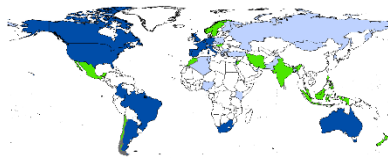
Exhibition of "How do you C me" (March 2018 in London) of the association Caring Matters Now remains an exhibition that will have marked the spirits and we hope to see it export and begin its round-the-world, as it changes the way the general public can put on the CMN and thus limit the stigma factor mentioned in the first article .

Patient Associations Report

Written by Marjolein van Kessel (Leader of NI Patient Support Group Network)

1. Patient Advocacy team Naevus International/Naevus Global

- New networks for Africa, the Nordic countries, Hispanic North America, and Arabic countries.
- 35 countries connected (see colors on map)!
- The newest Facebook group in Ukraine!
- Patient advocacy in Kenya
- Naevus Global is formalized as an official organization for patient advocacy



Ukraine

2. International activities 2019 Advocacy and Awareness for CMN



2a. Caring Matters Now exhibition 'how do you C Me Now?'

London, UK. March 2019 The Caring Matters Now exhibition 'how do you C Me Now?' at the gallery@oxo Oxo Tower Wharf. The exhibition featured 30 inspirational individuals affected by Congenital Melanocytic Naevi (CMN). The global media coverage has been phenomenal. They have welcomed over 8,000 visitors to the gallery!

2b. MPNE (Melanoma Patient Network Europe) conference

Brussels, Belgium March 2019 Marjolein van Kessel Attended the MPNE (Melanoma Patient network Europe conference) 2019. It helps connecting to Eastern European countries for CMN, connecting Nordic countries (in the benefit for CMN), connecting researchers worldwide, learning about the latest concepts in immunotherapy and access to innovative therapies. Also, she was inspired on how to organize patient advocacy. At the conference, she had the chance of presenting Naevus International on a poster session.



2c. Eurordis membership meeting

Bucharest, Rumania May 2019 Marjolein van Kessel, 60 patient advocates were present among 275 members in total representing 860 rare disease patient organizations in 70 countries worldwide (28 EU).

Most interesting projects shared with patient advocates:

1. Patient journeys: making a template to structure the needs during different phases of a condition. It empowers patients with information and identifies the needs to show to clinicians.
2. Patient involvement in registration.
3. Registration of disease and their code in Orphanet and HPO (Human Phenotype Ontology) and how it works.
4. Establishing Patient Community Advisory Boards to offer patient expertise to clinical research.

2d. Global Skin

Milan, Italy, June 2019 Lauren Isbell and Marjolein van Kessel represented CMN at the Canadian Global Skin Foundation who organized two Congresses in Milan (Italy). Part of the congress was organized for representatives of rare skin disorders (RareDERM). The number of participants was 140 from 35 countries. The Global Skin Foundation was founded in 2015 and grows tremendously fast. Speakers came from all over the world and the range of subjects was broad and covered not only medical aspects but also genetic and psychosocial aspects. Global Skin is working on a collaborative project called GRIDD (Global Research on the Impact of Dermatological Diseases). It's a groundbreaking patient led impact research with questions in instrument developed by patients (not researchers). When developed and used patient experience data can be analyzed by country and disease.



2e. Team Naevus 2000 Ironman Vichy and charity dinner

August 25th-24th, Vichy France, The Team Naevus 2000 Ironman Vichy, (around 40 triathletes) came to Vichy with their family in order to participate to all different Ironman races under Naevus 2000 colors !

Thanks to all of them, we improved awareness of Naevus, we informed about it, in front of 40 000 visitors/participants!

Thanks to this donation, Naevus 2000 organized a Charity dinner at cité de l'automobile - musée national collection schlumpf in Mulhouse. During that event 24 chefs of the National Cooking Academy, voluntarily prepared a delicious gourmet dinner served to 313 guests.

The benefits of this charity dinner will be mainly donated to research on the Congenital Giant Nevus, and more specifically to the team of Heather Etchervers, researcher at Inserm in Marseille. Another part will be reserved for the organization of family reunions and social actions in favor of affected children.

Video: <https://fbwat.ch/161rRjN23i2RJ7QY>

2f. Naevus International meeting

September, Brussels, Belgium Naevus International meeting combined with a meeting for patient advocates worldwide. For Naevus International presentations see www.naevusinternational.com



2g. Annual meeting French support group

Paris, October 5th 6th. Naevus 2000 had their annual meeting at Village Nature Paris, where 40 families/150 participants joined their event with a medical conference in the afternoon where kids learned psychosocial adjustment strategies "EN PISTE" and E-R & D through a game in the land of the Cékikis with the precious support of Association Anna, followed by an altogether dinner in the evening, rich in exchanges and meetings.



2h. MPNE conference for rare melanoma

Berlin, October 19th – 21st 2019 Benjamin Blume had the opportunity to do a presentation on CMN: melanoma related to CMN. There were ten different sessions at the conference. MPNE wants rare melanoma's (like melanoma in CMN) to use the fully available network for melanoma and one of their main aims is to share their knowledge for patients and patients advocates.

2i. NORD conference USA (National Organization Rare Disorders)

Washington DC, October 20th -22nd 2019 Marjolein van Kessel attended their annual congress with around 900 participants. There was a special session organized for Patient Leaders. The conference consisted mainly of panel discussions. The panels consisted of a wide variety of participants with different backgrounds such as patient organizations, the US Food & Drug Administration (FDA), pharmaceutical companies, National Institute of Health (NIH) and NORD.

2j. ICORD conference, Tel Aviv, Israel



Tel Aviv, December 12th and 13th, 2019, Inbal Engler, From the Israeli Nevus Support group attended the ICORD, which is an International Society for all individuals active in rare diseases and/or orphan drugs. During recent decades, the awareness on problems associated with Rare Diseases has increased markedly. Moreover, the international collaboration on Rare Diseases has improved. However, there are still many unmet needs for patients with Rare Diseases, not least in developing countries. Experts in rare diseases from academia, patient's organizations, industrial developers, and government policy makers and regulators from Europe, North and South America, Asia and Africa lectured on the following:

- Recent rare diseases research
- Genetic development in exposing and treating genetic disorders
- Importance of big data as a key of discovering, tracking curing rare diseases.
- Social security approach and methodologies to define rare diseases among children and grant monthly allowances.
- Joint efforts with industrial developers' companies to search for a cure

Patient group advocates gave tips on how to increase awareness, showed how connecting globally help empowering the organizations, challenges and tips. Proud to be the ambassador of Nevus organizations! Rare Diseases Are Not Orphans!

2k. ERN (European Reference Network) training session



Gent, Belgium, December 16th Marjolein Vankessel was invited to participate in a panel for an ERN training session within the European Reference Network (European rare skin disorders). At the training, the newest findings on CMN were discussed, as well as other rare skin conditions. The audiences were doctors and professors from various countries with both medical and genetic backgrounds. Prof. Dr. Kinsler gave a presentation. Together with 3 other patient advocates, we were asked to discuss 'patient burdens in rare skin disorders - what do physicians need to know?'. It was the first-time patient representatives were asked to join a meeting like this for a panel discussion. We were honored to be given this opportunity!

"NOTHING ABOUT US, WITHOUT US"

3. Research project OCOMEN

On the 21st of January 2020, the Outcomes in Congenital Melanocytic Nevi (OCOMEN) research team organized an online consensus meeting to decide what outcomes should be measured in congenital melanocytic nevi (CMN) research and care.

A total of 33 participants from all over the world, participated in the online meeting including: persons with CMN, parents, dermatologists, pediatric surgeons, neurologist, pathologist, and psychologist. During this meeting, participants discussed what outcomes should be included in a so called 'Core Outcome Set'. This are the outcomes that should always be measured in all research and/or care of CMN.

What is a Core Outcome Set and why is it important?

At the moment, different studies evaluating treatment of CMN often measure different outcomes. For example: imagine 2 studies of laser treatment for CMN.

Study A - researchers measure the color of CMN

Study B - researchers measure the number of complications

When the two studies are finished, we cannot compare or combine their results because they have used different outcomes.

In addition to research, outcomes measured in care of CMN are also different. Therefore, the care provided for CMN is not the same in different medical centers.

What is the solution?

If all studies and clinical centers used the same set of outcomes, they could all be compared and combined. This will improve research and will make the care uniform in different medical centers. The name of this set of outcomes is a 'Core Outcome Set'.

Development Core Outcome Set

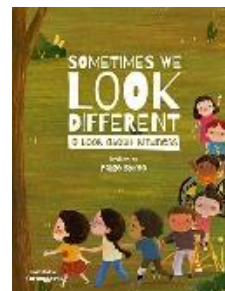
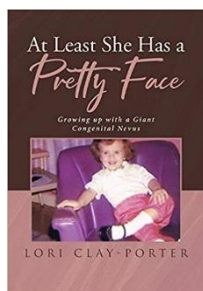
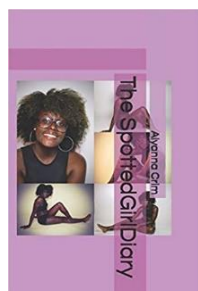
Last year, persons with CMN/parents and professionals voted what domains are important in CMN research and care (table 1). In the online consensus meeting on January 21st 2020 participants discussed what specific outcomes should cover these domains.

Table 1: Core domains of the core outcome set for clinical care and research.

No	Domains for clinical care	Domains for research
1	Quality of life (including social, family, emotional and physical function)	Quality of life (including emotional function)
2	Neoplasms	Neoplasms
3	Nervous system	Nervous system
4	Anatomy of the skin	Anatomy of the skin
5	General adverse events	Pathology

The participants will give their final vote in the last week of January. The next stem of the OCOMEN project is to decide what outcome measurement instruments should be used to measure the outcomes of the Core Outcome Set.

4. Books published



Sometimes We Look Different, Paige Byrne

This book was written by a mom whose second child was born with a CMN covering a large part of her face. The purpose of this book is to bridge that gap taking a very kid-friendly approach to explaining visible differences, kindness, and what to do when you see someone who looks differently than you.

At Least She Has a Pretty Face: Growing up with a Giant Congenital Nevus, by Lori Clay-Porter

Most of her friends don't even know she has a birthmark. The book is titled: "At Least She Has a Pretty Face". Her deepest wish would be for this book to help not only people born with a CMN, but also to inspire all people born with unusual birth defects or obstacles in life. Also, to help parents coping with children born with nevus or other related conditions. She is living a fantastic life with many adventures which she shares in her book.

The Spotted Girl Diary (The Spotted Girl Diaries), Alyanna Renae' Crim and Sols Write House

The Spotted Girl Diaries is about a girl who lives with CMN. In her book she talks about her struggles and how I overcame it.