



CANADIAN NETWORK FOR IMPROVED OUTCOMES
IN SYSTEMIC LUPUS ERYTHEMATOSUS

CaNIOS

May 29, 2006

Judi Farrell, COO, Lupus Canada
590 Alden Road, Suite 211
Markham, Ontario L3R 8N2

Dear Ms. Farrell,

The Canadian Network for Improved Outcomes in SLE (CaNIOS) has enjoyed benefits from the collaboration with Lupus Canada and its financial support over the past years. I am writing to update you on this year exciting developments and progress made possible by your support of the CaNIOS National Registry. Appendix 1 provides a full detailed report of CaNIOS activities for 2005/2006.

As reported in 2004, CaNIOS has been able to obtain full funding for the position of the CaNIOS National Scientific and Development Coordinator through the Lupus Clinical Trials Consortium. The support from Lupus Canada that is matched yearly by a private donor through AARC Foundation has therefore been shifted to the positions of Administrative Coordinator and Database Manager/Administrator.

Our Database Manager/Administrator has been extremely busy in the past year in developing the basis and implementing the process to collect data nationally in our CaNIOS National Registry. Accomplishments that are a direct result of having this position are many. The Database Manager created, launched and maintains our web presence through our new website, www.canios.ca. We have: 1) established the CaNIOS National Registry that has started being populated by data from different CaNIOS centres across Canada; 2) created a clinical/research database software that has been distributed to CaNIOS members that did not have a database and that will be made available to our new members; and 3) ensured that our CaNIOS Privacy Code be up to date and adhered to at every level of CaNIOS data storage and transfer. The Database Manager was the link with vendors and service providers and has been responsible for site visits, reviewing processes and managing the projects from inception to implementation and follow-up. You will find in Appendices 2 and 3 tables that update you on the data collected so far for the years 2002 to 2005. This is now growing rapidly as we train and bring on board those centres that did not have an existing database. To follow is a summary of our achievements as reported to the Arthritis and Autoimmunity Research Centre Foundation.

CaNIOS National Lupus Registry, Database software and Privacy Code

The goals of the National Registry are to describe SLE in the Canadian population, to increase the power of medical research, and to exchange valuable clinical information between doctors and researchers. CaNIOS is therefore developing a platform that should attract interest from investigators planning prospective cohort studies and from companies starting new clinical trials in lupus in Canada. This unique central database allows for more than 25 individual centres to share data for projects of interest to all while remaining in control of their own data. A CaNIOS policy on intellectual property and a Privacy Code insures ownership of data by individual investigators and protection of their intellectual property on one part, and insures patient confidentiality in compliance with federal and provincial privacy legislations. While each centre can access the data from their own centre without restriction from CaNIOS, a process to access data from other CaNIOS centres has been developed and put in place in order to insure that data sharing is both secure and ethics board approved. To date, we have imported data from more than 1300 patients from five centres with existing local lupus databases including Toronto, Halifax, London, Montreal and Winnipeg.

Chair

Paul R. Fortin,
MD, MPH, FRCPC

Vice-Chair

Janet E. Pope,
MD, FRCPC

Secretary

C. Douglas Smith,
MD, FRCPC

Executive Member

Christine A. Peschken,
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National Scientific & Development Coordinator

Jaime O. Claudio,
PhD.

Business Administrator

Luciana Brown,
B.A.S.



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Dissemination and Knowledge Transfer

To date eight centres have been trained to utilize the new database. We have successfully used web conferencing to train study coordinators last December 15th for the 1000 Faces of Lupus/CaNIOS National Registry database program. Four CaNIOS Centres participated in the first wave of training including Centre 08 (SJHSC, London), Centre 10 (WHSC, Winnipeg), Centre 17 (TWH-CPSRD) and Centre 20 (SickKids, Toronto). A second wave of training held in January 2006 had four Centres participating: Centre 27 (Montreal Children's Hospital), Centre 21 (BC Children's Hospital), Centre 16 (McMaster University) and Centre 24 (Sunnybrook Hospital). If there is a need for more centres to receive training this will be organized through the Database Administrator at the coordinating centre.

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Since February 2006, 5 centres have uploaded their SLE cohort data into the CaNIOS National Registry. A sample of information that can be retrieved was presented at the 2006 Canadian Rheumatology Association meeting in Mexico. Appendix 2 and 3 contain tables of information that what can be generated by the data in the registry.

The Database Manager continues to work closely with the National Scientific and Development Coordinator and our service providers locally and nationally. We look forward to the continued progress we are making in this area and remain grateful to Lupus Canada and its Member Organizations for their funding of our database development.

Sincerely,

Paul Fortin, M.D., M.P.H., F.R.C.P.(C)
Director of Clinical Research - Arthritis Centre of Excellence
UHN - Toronto Western Hospital

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Enclosure – CaNIOS 2005/2006 Update

Appendix 1

CaNIOS 2005/2006 Update for Lupus Canada

The past year has been a banner year for CaNIOS. CaNIOS achieved a milestone that any organization with humble beginning should be very proud of - it celebrated a decade long of achievements in lupus research. From its inception as a network in 1995 with the Study of Methothrexate in Lupus Erythematosus (SMILE), CaNIOS has indeed grown into a truly national collaborative network of clinicians and scientists studying lupus in Canada. The following are CaNIOS achievements in the past year:

1 . CaNIOS National Lupus Registry, Database software and Privacy Code

The goals of the National Registry are to describe SLE in the Canadian population, to increase the power of medical research, and to exchange valuable clinical information between doctors and researchers. CaNIOS is therefore developing a platform that should attract interest from lupus investigators and companies starting new clinical trials in lupus in Canada. This unique central database allows for more than 25 individual centres to share data for projects of interest to all while remaining in control of their own data. A CaNIOS policy on intellectual property and a Privacy Code ensures ownership of data by individual investigators and protection of their intellectual property on one part, and ensures patient confidentiality in compliance with federal and provincial privacy legislations. While each centre can access the data from their own centre without restriction from CaNIOS, a process to access data from other CaNIOS centres has been developed and put in place in order to ensure data sharing is both secure and ethics board approved. To date, we have imported data from 5 centres with existing local lupus databases including Toronto, Halifax, London, Winnipeg and Montreal. Our database has become a model system for other disease groups such as Scleroderma (CSRG) and spondylitis (SPARCC). By sharing our expertise, we hope to not only encourage research collaboration but also provide us with a more efficient cost-saving shared core infrastructure.

We are providing you in appendix 2 the most recent table from our CaNIOS National Lupus Registry. Patient demographics in the appended Tables are from 5 centres. We expect to have over 2,000 patients registered once data from other centres participating in the 1000 Faces of Lupus start to populate our National Lupus Registry by the third quarter of 2006.

In order to facilitate CaNIOS centres without an existing program to deposit their cohort data into the National Registry, CaNIOS has recently developed a National Database program that is currently distributed free of charge to these CaNIOS centres. This computer program will not only allow other centres to efficiently and annually upload their data into the CaNIOS National Registry, but more importantly, will enable each centre to develop a database of their own. Of special benefit to this endeavor are small academic based clinics and community-based rheumatology clinics that otherwise would not have the resources to develop their own database.

2. Ongoing research activities and successful new grant competition

Since 2003, four research studies have been funded and coordinated at the CaNIOS Coordinating Centre in Toronto: (a) HIPP, a randomized controlled trial aimed at comparing the Health Improvement and Prevention Program versus usual care with the goal of improving health status, decreasing cardiovascular risk and improving endothelial function in persons with lupus. (b) ThromboFIL studies factors that increase the chances of developing a blood clot in persons with lupus. (c) GenES is a research program to identify genes, environmental factors, and gene-environment interactions that influence the risk of lupus. (d) 1000 Canadian Faces of Lupus aims to establish a longitudinal multi-ethnic Canadian lupus cohort to characterize ethnic differences in clinical manifestations and disease outcome.

A new study, LuNNET, was funded by the Canadian Institutes of Health Research in the fall of 2005. LuNNET (Lupus Nephritis – New Emerging Team) unites a nation-wide team of experts with unique expertise working towards the discovery and definition of the mechanisms that lead to disease expression and damage in lupus nephritis, an inflammation of the kidneys that may lead to kidney failure in lupus. Once again, CaNIOS was instrumental in bringing experts from various research backgrounds to apply their knowledge to the area of lupus with the expectation to improve treatments of this condition in the near future.

3. SARD Conference

As the driving force in the planning of the SARD Conference, CaNIOS played a pivotal role in defining unmet needs, and pushing strategic priorities and research agenda in SARD. The goal of the SARD conference held in Toronto on December 3-4 was to identify new opportunities and research priorities in Canada for academia, government, industry, professional organizations and patients to work together. Subsequently, CaNIOS maintains a major role in advancing plans for partnership with other groups, such as the Allergy, Genes and Environment Network - National Centre of Excellence (AllerGEN NCE), the Canadian Scleroderma Research Group (CSRG), the Canadian Arthritis Network (CAN) and other organizations, to support the growth of SARD Research.

4. Lupus Health Passport

The Lupus Health Passport (LHP) is a recent project developed as a tool to administer and monitor the complex interventions of the Health Improvement and Prevention Program. Through financial support from the Mclean Foundation, Lupus Ontario, and the Arthritis and Autoimmunity Research Centre Foundation (AARCF), the initial phase of passport development by dedicated lupus nurses Anne Cymet in Toronto and Carolyn Neville in Montreal have led to a passport prototype that is undergoing pilot testing with lupus patients. The Passport is designed to be filled out by a nurse who works together with a lupus patient to record contact information, medication, blood test results, personalized health care plan, annual screening schedule, and general helpful tips. While it is currently only used by the HIPPP study, it is hoped that the Lupus Health Passport will become part of the standard of care for lupus patients in the future. In order to safeguard our intellectual property, copyright application has been initiated through the Research Business Development Office of the University Health Network.

5. CaNIOS website and visual branding

In 2005, CaNIOS registered two domain names it calls its own: CaNIOS.org and CaNIOS.ca. The CaNIOS website (www.CaNIOS.ca or www.CaNIOS.org) was launched in the summer as the site to find more about CaNIOS and the place to unite all centres, clinicians, researchers, and principal investigators under CaNIOS to exchange information. It is also a site designed for the public to know more about the network and how they can participate in several clinical studies.

In working with a graphic design company for the blueprint of the Lupus Health Passport, we seized the opportunity to develop a visual identity unique to CaNIOS. The color motif and butterfly designs have become integral to the artwork done for the LHP, the CaNIOS Brochure, and PowerPoint slide templates. The same concept will be carried over for our website and letterheads in the coming months. As our network matures, branding has become indispensable means towards added public awareness and name recognition to our network.

6. Mentorship

CaNIOS continues to attract new membership with two active members and one trainee. This year, Dr. Raja Bobba who was an investigator trainee at CaNIOS Centre 17 (TWH) has moved to McMaster University's St Joseph Health Care (CaNIOS Centre 16) to establish his independent research in lupus.

Together with Dr. Sasha Bernatsky in Montreal, their success is testament to the commitment of CaNIOS in providing mentorship to young investigators in lupus research. Likewise, the CaNIOS mentorship program of undergraduate students through the CRA-Merck Summer Studentship has led to an award-winning research abstract by Emily Kelly during the joint Mexican-Canadian Rheumatology Meeting in Acapulco in February 2005.

7. Partnership with Lupus Canada

The relevance of CaNIOS as an organization is measured by its interactions with stakeholders. As in the past years, our combined annual meeting with Lupus Canada has become an important means of strengthening our partnership. This meeting has not only provided a venue for scientific networking among CaNIOS members, but more so as an opportunity for lupus patients to know more about the disease from expert clinician scientists and to get emotional, social, and psychological support through interaction with other patients. This year, CaNIOS and Lupus Canada partnered together in raising funds for the annual meeting in Halifax.

8. New Employees

In October 2005 Dr. Jaime O. Claudio joined CaNIOS as the National Scientific and Development Coordinator after Ms. Diane Ferland left the position of National Coordinator in July 2005. Dr. Claudio also acts as CaNIOS Privacy officer and serves as coordinator for CaNIOS scientific activities, and the development of new projects. In the same month, Dr. Thulassi Unnithan was hired as LuNNET national coordinator. Ms. Lisa Zeng was recruited in mid September 2005 as full time laboratory technician responsible for processing and proper storage of blood, serum and plasma samples of lupus patients from Toronto clinics and from other CaNIOS centres.

9. Research Highlights, Publications and Abstracts

Three abstracts submitted for presentation to the Annual Scientific Meeting of the American College of Rheumatology in November 2006 highlight our progress in improving the health status of persons with lupus and in studying the genetic and environmental factors in SLE. An abstract reporting preliminary results from the HIPP study which is aimed at teaching lupus patients to live better with the disease was submitted. Interestingly as well, in looking for genetic variants within 8 candidate genes, the GenES study identified two single nucleotide polymorphisms (SNP) in the *LY9* locus with an increased association with SLE. This positive preliminary finding, although requiring replication before making a solid conclusion, proves that our collection of DNA materials from lupus patients and their family members is a goldmine in our genomic approach to pinpoint genetic risk factors in lupus. It is a significant and unique resource afforded to us by supportive lupus patients and their families. In a related GenES study, analysis of autoantibodies from serum samples of parents and siblings of lupus patients showed an increased frequency of anti-nuclear antibodies (ANA) when compared to population controls. The presence of a positive ANA is associated with a reduced proportion of NKT cells – a specialized type of immune cell, suggesting that this cell subset plays a role in the regulation of anti-nuclear autoantibody production. The 1000 Faces of Lupus study is nearing its recruitment target through the robust support of multi-ethnic research participants all over Canada. The LuNNET national collaborative platform of uniting a wide array of expertise to dissect the genetic, biochemical and environmental factors associated with the development of lupus nephritis has also made headway in its initial stages of patient recruitment.

In 2005 CaNIOS members authored and edited the revised edition of the book: "Lupus - The Disease with 1,000 Faces" (see appended copy of the book cover). A total of 5 peer-reviewed research studies were published in 2005 and 3 studies were presented at the American College of Rheumatology Meeting held in San Diego in November 2005. The citations for these studies are appended in this report.

2005 Publications by CaNIOS Members

Published/in press peer-reviewed manuscripts:

1. Bernatsky S, Ramsey-Goldman R, Boivin J-F, Joseph L, Rajan R, Zoma A, Manzi S, Ginzler E, Urowitz M, Gladman D, Fortin PR, Petri M, Edworthy E, Barr S, Gordon C, Bae S-C, Sibley J, Isenberg D, Rahman A, Aranow C, Dooley M-A, Steinsson K, Nived O, Sturfelt G, Alarcon G, Senecal J-L, Zummer M, Hanly J, Ensworth S, Pope J, El-Gabalawy H, McCarthy T, St. Pierre Y, Clarke A. An international cohort study of cancer in systemic lupus erythematosus (SLE). Arthritis and Rheumatism 2005;52(5):1481-90. (coll)
2. Shariati Sarabi Z, Chang ER, Bobba RS, Ibanez D, Gladman D, Urowitz M, Fortin PR. The incidence rates of arterial and venous thrombosis after diagnosis of systemic lupus erythematosus. Arthritis Care and Research 2005, 53:609-12. (coll).
3. Bernatsky S, Boivin J-F, Joseph L, Manzi S, Ginzler E, Urowitz M, Gladman DD, Fortin PR, Gordon C, Barr S, Edworthy S, Bae S-C, Petri M, Sibley J, Isenberg D, Rahman A, Steinsson K, Aranow C, Dooley MA, Alarcón G, Hanly J, Sturfelt C, Nived O, Pope J, Ensworth S, Rajan R, El-Gabalawy H, McCarthy T, St. Pierre Y, Clarke A, Ramsey-Goldman R. Race/Ethnicity and cancer occurrence in systemic lupus erythematosus. Arthritis & Rheumatism. 2005;53(5):781-784. (coll)
4. Bernatsky S, Ramsey-Goldman R, Rajan R, Boivin J-F, Joseph L, Lachance S, Cournoyer D, Zoma A, Manzi S, Ginzler E, Urowitz M, Gladman DD, Fortin PR, Edworthy S, Barr S, Gordon C, Bae S-C, Steinsson K, Sturfelt C, St. Pierre Y, Clarke A. Non-Hodgkin's lymphoma in systemic lupus erythematosus. Ann Rheum. Dis. 2005;64:1507-1509. (coll)
5. Chagnon P, Schneider R, Herbert J, Fortin PR, Provost S, Bellisle C, Gingras M, Bolduc V, Perreault C, Silverman E, Busque L. Identification and characterization of an Xp22.33 ; Yp11.2 translocation causing a triplication of several genes of the PAR1 region in an XX male patient with severe systemic lupus erythematosus. (conditional acceptance to Arthritis & Rheumatism- July 2005) (coll).

Abstracts:

1. Bernatsky S, Boivin J-F, Joseph L, Rajan R, St. Pierre Y, Ramsey-Goldman R, Clarke AE, Systemic Lupus International Collaborating Clinics (SLICC), Canadian Network for Improved Outcomes in Systemic Lupus Erythematosus (CaNIOS). Mortality in systemic lupus erythematosus: Risk according to cause, age, sex and lupus duration. American College of Rheumatology, 2005. San Diego, CA, November 2005.
2. Bernatsky S, Boivin J-F, Joseph L, Rajan R, St. Pierre Y, Ramsey-Goldman R, Clarke AE, Systemic Lupus International Collaborating Clinics (SLICC), Canadian Network for Improved Outcomes in Systemic Lupus Erythematosus (CaNIOS). The Influence Of Geographical And Racial/ethnic Factors On Mortality Risk In Systemic Lupus Erythematosus. American College of Rheumatology, 2005. San Diego, CA, November 2005.
3. Bernatsky S, Boivin J-F, Joseph L, Rajan R, St. Pierre Y, Ramsey-Goldman R, Clarke AE, Systemic Lupus International Collaborating Clinics (SLICC), Canadian Network for Improved Outcomes in Systemic Lupus Erythematosus (CaNIOS). Trends in relative mortality rates for systemic lupus erythematosus over calendar time. American College of Rheumatology, 2005. San Diego, CA, November 2005.



Appendix 2

Recruitment Statistics for Current CaNIOS Studies (Updated May 2006)

1000 Faces of Lupus – Enrolled = 783*	
Centre 07 Ottawa Hospital	10
Centre 08 London	98
Centre 10 Winnipeg HSC	198
Centre 17 TWH CPSRD	369* (pending)
Centre 19 TWH Non-CPSRD	35
Centre 20 SicKids, Toronto	28
Centre 21 BC Children's Hosp.	38
Centre 27 Montreal Child. Hosp.	7
Centre 30 Calgary's Child. Hosp.	new
Centre 31 Hos. Ste. Justine	new

GenES – Blood collection completed = 183 Trios	
Centre 01 MGH	21
Centre 03 ND	10
Centre 06 QEII Halifax	15
Centre 07 Ottawa	12
Centre 08 London	37
Centre 09 Calgary	1
Centre 10 Winnipeg	8
Centre 12 Sherbrooke	4
Centre 17 TWH CPSRD	70
Centre 19 TWH non CPSRD	4
Centre 23 St. Michael's	0
Centre 24 Sunnybrook	0
Centre 25 Halifax Non-QEII	1
Centre 28 Mt. Sinai	0

ThromboFIL – Enrolled = 282	
Centre 01 MUHC	60
Centre 08 London	36
Centre 10 Winnipeg	12
Centre 12 Sherbrooke (N=18)	1
Centre 17 TWH-CPSRD	167
Centre 19 TWH –non CPSRD	6

HIPP – Currently enrolled = 144	
Centre 01 MGH (N=38)	91
Centre 17 TWH-CPSRD	51
Centre 19 TWH-Non CPSRD	2



Demographics in the CaNIOS Registry for years 2002-2005 (as of May 24, 2006)

CaNIOS Centre	Frequency	Percent
Centre 01 MGH	350	26.14
Centre 06 QEII Halifax	169	12.62
Centre 08 London	22	1.43
Centre 10 Winnipeg	121	9.04
Centre 17 TWH CPSRD	577	50.56
Total no. of patients	1339	100.00

Gender	Percent
Female	87.36
Male	12.64

Ethnicity	Percent
Aboriginal	2.51
Asian	10.60
Black	8.95
Hispanic/Latino	0.63
White	72.68
Other	3.69
Mixed	0.94
Total	100.00