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InFACT –
a network of ICU networks

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InFACT

- International Forum for Acute Care Trialists

InFACT
International Forum for Acute Care Trialists

www.infactglobal.org

InFACT

- Alliance of investigator-led clinical research groups
- Focus is the optimal management and care of critically ill adults and children worldwide
- Aiming to support, integrate and promote greater international collaboration in investigator-led critical care research by facilitating collaboration and co-operation
- Network of autonomous member groups with no aim to supplant or control its individual members

InFACT
International Forum for Acute Care Trialists

InFACT – brief history (i)

- InFACT initiated by John Marshall
- Emergence of investigator-led critical care research groups e.g.
  - CCCTG 1989
  - ANZICS CTG 1994
  - ARDSNet 1994
  - Etc.

CCCTG

- Small beginnings, now…
  - 300+ members
  - ~50 active research studies
  - High success rate with funders
  - Entirely self-funded
  - No infrastructure

The New England
Journal of Medici

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VOLUME 340 FEBRUARY 11, 1999

A MULTICENTER, RANDOMIZED, CONTROLLEI
OF TRANSFUSION REQUIREMENTS IN CRI

PAUL C. HÉBERT, M.D., GEORGE WELLS, PH.D., MORRIS A. BLAJCHMAN, M
CLAUDIO MARTIN, M.D., GIUSEPPE PAGLIARELLO, M.D., MARTIN TWEEDDALE, M.D
ELIZABETH YETISIR, M.SC., AND THE TRANSFUSION REQUIREMENTS IN CRI
FOR THE CANADIAN CRITICAL CARE TRIALS GROU

The NEW ENGLAND JOURNAL of MEDICINE

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ORIGINAL ARTICLE

Volume 330:377-381 February 10, 1994 Number 6 Next ▶

Risk Factors for Gastrointestinal Bleeding in Critically Ill Patients

Deborah J. Cook, Hugh D. Fuller, Gordon H. Guyatt, John C. Marshall, David Leasa, Richard Hall, Timothy L. Winton, Frank Rutledge, Thomas Todd, Peter Roy, Jacques Lacroix, Lauren Griffith, Andrew Willan, for The Canadian Critical Care Trials Group

ESTABLISHED IN 1812 JANUARY 2, 2003 VOL. 348 NO. 1

A Randomized, Controlled Trial of the Use
of Pulmonary-Artery Catheters in High-Risk Surgical Patients

James Dean Sandham, M.D., Russell Douglas Hull, M.B., B.S., Rollin Frederick Brant, Ph.D.,
Linda Knox, R.N., Graham Frederick Pineo, M.D., Christopher I. Doig, M.D., Denny P. Laporta, M.D.

ORIGINAL ARTICLE

The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 20, 2003 VOL. 348 NO. 8

Withdrawal of Mechanical Ventilatio
Anticipation of Death in the Intensive Ca

One-Year Outcomes in Survivors
of the Acute Respiratory Distress Syndrome

Margaret S. Herridge, M.D., M.P.H., Angela M. Cheung, M.D., Ph.D., Catherine M. Tansey, M.Sc.,
Andrea Matte-Martyn, B.Sc., Natalia Diaz-Granados, B.Sc., Fatma Al-Saidi, M.D., Andrew B. Cooper, M.D.,

The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 21, 2006 VOL. 355 NO. 25

A Randomized Trial of Diagnostic Techniques
for Ventilator-Associated Pneumonia

The Canadian Critical Care Trials Group*

The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 19, 2007 VOL. 356 NO. 16

Transfusion Strategies for Patients
in Pediatric Intensive Care Units

Jacques Lacroix, M.D., Paul C. Hébert, M.D., James S. Hutchison, M.D., Heather A. Hume, M.D.,
Marisa Tucci, M.D., Thierry Ducruet, M.Sc., France Gauvin, M.D., Jean-Paul Collet, M.D., Ph.D.,
Baruch J. Toledano, M.D., Pierre Robillard, M.D., Ari Joffe, M.D., Dominique Biarent, M.D.,

Investigator-led Critical Care Trials Groups

InFACT – brief history (ii)

- Informal discussions at conferences including World Federation 2005
- "Born" at a meeting in Granada, Spain in late 2008
- H1N1 pandemic 2009 galvanised nascent (some might say non-existent…?!) organisation into action

InFACT – H1N1

- 22 investigator-led research groups agreed to join an urgent, unprecedented global research collaboration

InFACT: a global critical care research response to H1N1

The H1N1 pandemic presents acute care researchers with an extraordinary challenge and an unprecedented opportunity. By early October, 2009, there had been more than 340 000 reported cases of H1N1 infection in 191 countries, with more than 4100 deaths.[1] WHO initially projected that up to 2 billion people could become infected with the virus over the next 2 years.[2] Although vaccination programmes and other factors should reduce this number, plausible estimates of the number of infected individuals who might benefit from admission to intensive care range from 200 000 to 10 million. Influenza killed at least 50 million people during the 1918 pandemic.[3] Today, with antibiotics and antiviral agents, mechanical ventilation, and the supportive measures available in intensive care, most of those deaths could have been prevented.

The mortality for H1N1-infected patients admitted to intensive care ranges from 10 to 40% over the first month,[4–8] and survivors spend a median of 2 weeks in the intensive care unit. To reduce this toll requires a better understanding of the epidemiology and clinical biology of the disease, and the identification of effective management strategies. New knowledge must be gathered with unprecedented speed and efficiency. Beyond antiviral agents, anecdotal reports and data from animal studies suggest that illness severity can be attenuated by readily available agents, such as corticosteroids and statins, that can modulate the host's inflammatory response.[9] None of these drugs has been adequately studied for efficacy.

It is within the intensive care unit that the most severely affected patients will be treated. As international leaders of investigator-led clinical research consortia, and as clinicians dedicated to the care of critically ill patients, we have joined together as the

Panel: The InFACT H1N1 Research Collaborative

Collaborating investigator-led research groups:

- Australia and New Zealand Intensive Care Society Clinical Trials Group (ANZICS CTG)
- ANZICS Paediatric Study Group (ANZICS PSG)
- Acute Respiratory Distress Syndrome Network (ARDSnet)
- Canadian Critical Care Trials Group (CCCTG)
- European Critical Care Research Network (ECCRN) Trials Group
- German Sepsis Society (DSG)
- Gruppo Italiano per la Valutazione degli Interventi in Terapia Intensiva (GiViTI)
- Intensive Care National Audit and Research Centre (ICNARC)
- Intensive Care Society Trials Group
- Irish Critical Care Trials Group (ICCTG)
- Latin American Sepsis Institute
- Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network
- Protocolized Care for Early Septic Shock (ProCESS) Investigators
- Scandinavian Critical Care Trials Group (SCCTG)
- Scottish Critical Care Trials Group (SCCTG)
- Sepsis Occurrence in Acutely Ill Patients (SOAP) Investigators
- Spanish Society of Critical Care Medicine H1N1 Registry (SEMICYUC WG)
- Swine Flu Triage Study Investigators (SWIFT)
- The George Institute for International Health
- United States Critical Illness and Injury Trials Group (USCIITG)

Professional societies:

- American Academy of Pediatrics, Section on Critical Care
- American Association of Critical Care Nurses (AACN)
- Canadian Critical Care Society (CCCS)
- Chilean Society of Intensive Medicine (SOCHIMI)
- College of Intensive Care Medicine of Australia and New Zealand
- Ecuadorian Society of Intensive Care (SECI)
- European Society of Intensive Care Medicine (ESICM)
- German Interdisciplinary Association of Critical Care Medicine (DIVI)
- German Society of Anesthesia and Intensive Care Medicine (DGAI)
- German Society of Medical Intensive Care Medicine (DGIIN)
- Indian Society of Critical Care Medicine (ISCCM)
- Intensive Care Society (ICS), UK
- International Pan Arab Critical Care Medicine Society (IPACCMS)
- Korean Society of Critical Care Medicine (KSCCM)
- Mexican Society of Intensive and Critical Care Medicine (AMMCTI)
- Pan-American and Iberic Federation of Critical Care Medicine (FEPIMCTI)
- Scottish Intensive Care Society (SICS)
- Society of Intensive Care Medicine, Singapore (SICM)
- Society of Critical Care Medicine (SCCM)
- Surviving Sepsis Campaign (SSC)
- World Federation of Societies of Intensive and Critical Care Medicine (WFSICCM)
- World Federation of Pediatric Intensive and Critical Care Societies (WFPICCS)

InFACT – H1N1

- 22 investigator-led research groups agreed to join an urgent, unprecedented global research collaboration
- Promoted collaboration between H1N1 registries e.g. CCCTG, ANZICS CTG, ARDSNet, ICNARC, ESICM, etc.

Early observational research and registries during the 2009–2010 influenza A pandemic

Robert A. Fowler, MD, MS; Steven A. R. Webb, MD, MPH, PhD; Kathy M. Rowan, PhD; Charles L. Sprung, MD; B. Taylor Thompson, MD; Adrienne G. Randolph, MD, MSc; Philippe Jouvet, MD, PhD; Stephen Lapinsky, MB, BCh; Lewis Rubinson, MD, PhD; Jordi Rello, MD, PhD; J. Perren Cobb, MD; Todd W. Rice, MD; Tim Uyeki, MD; John C. Marshall, MD

As a critical care community, we have an obligation to provide not only clinical care but also the research that guides initial and subsequent clinical responses during a pandemic. There are many challenges to conducting such research. The first is speed of response. However, given the near inevitability of certain events, for example, viral respiratory illness such as the 2009 pandemic, geographically circumscribed natural disasters, or acts of terror, many study and trial designs should be preplanned and modified quickly when specific events occur. Template case report forms should be available for modification and web entry; centralized research ethics boards and funders should have the opportunity to preview and advise on such research beforehand; and national and international research groups should be prepared to work together on common studies and trials for common challenges. We describe the early international critical care research response to the influenza A 2009 (H1N1) pandemic, including specifics of observational study case report form, registry, and clinical trial design, cooperation of international critical care research organizations, and the early results of these collaborations. (Crit Care Med 2010; 38[Suppl.]:e120–e132)

Key Words: critical care; intensive care; registry; H1N1; influenza; pandemic

InFACT – H1N1

- 22 investigator-led research groups agreed to join an urgent, unprecedented global research collaboration
- Promoted collaboration between H1N1 registries e.g. CCCTG, ANZICS CTG, ARDSNet, ICNARC, ESICM, etc.
- Working groups formed:
  - Database: pooling H1N1 registries
  - Clinical trials – launched 3 trials

InFACT H1N1

- STIP Trial Rosuvastatin versus placebo
  USA: Gordon Bernard, PI

- CortiFlu Hydrocortisone versus placebo
  France: Djillali Annane, PI

- CHAT Trial Rosuvastatin versus placebo
  Canada: Karen Burns, John Marshall, PIs

InFACT – H1N1

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- Working groups formed:
  - Database: pooling H1N1 registries
  - Clinical trials – launched 3 trials
  - Ethics – challenges of pandemic research

Clinical research ethics for critically ill patients: A pandemic proposal

Deborah Cook, MD; Karen Burns, MD; Simon Finfer, MD; Niranjan Kissoon, MD, FCCM; Satish Bhagwanjee, MD; Djillali Annane, MD; Charles L. Sprung, MD, JD, FCCM; Rob Fowler, MD; Nicola Latronico, MD; John Marshall, MD

Pandemic H1N1 influenza is projected to be unprecedented in its scope, causing acute critical illness among thousands of young otherwise healthy adults, who will need advanced life support. Rigorous, relevant, timely, and ethical clinical and health services research is crucial to improve their care and outcomes. Studies designed and conducted during a pandemic should be held to the same high methodologic and implementation standards as during other times. However, unique challenges arise with the need to conduct investigations as efficiently as possible, focused on the optimal outcome for the individual patient, while balancing the need for maximal societal benefit. We believe that clinical critical care research during a pandemic must be approached differently from research undertaken under nonemergent circumstances. We propose recommendations to clinical investigators and research ethics committees regarding clinical and health services research on pandemic-related critical illness. We also propose strategies such as expedited and centralized research ethics committee reviews and alternate consent models.
(Crit Care Med 2010; 38[Suppl.]:e138–e142)

Key Words: critical care; pandemic; H1N1 influenza; clinical trials; research ethics committee; informed consent

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- Working groups formed:
  - Database: pooling H1N1 registries
  - Clinical trials – launched 3 trials
  - Ethics – challenges of pandemic research
  - Capacity – global capacity for critical care
  - Biologics – specimen collection for studies

InFACT – brief history (iii)

- H1N1 pandemic relatively short-lived
- Acted as a catalyst to launch InFACT
- *Interim* Executive Committee *very informally* formed:
  - Chair: John Marshall
  - Vice-Chair: Steve Webb
  - Secretary: Kathy Rowan
  - Treasurer: Derek Angus

- Confirmation of member organisations – *ongoing and growing…*

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InFACT – member organisations

- ANZICS CTG
- ARDSNet
- BRICNet
- CCCTG
- CRISMA
- ESICM CTG
- George Institute
- GiViTI
- Hellenic Sepsis Society
- ICNARC
- ICS UK
- Irish CCTG
- Kompetenznetz Sepsis
- Latin American Sepsis Institute
- Scandinavian CCTG
- Scottish CCTG
- United States Critical Illness and Injury Trials Group

InFACT
International Forum for Acute Care Trialists

InFACT – brief history (iii)

- H1N1 pandemic relatively short-lived
- Catalyst to launch InFACT
- *Interim* Executive Committee formed:
  - Chair: John Marshall
  - Vice-Chair: Steve Webb
  - Secretary: Kathy Rowan
  - Treasurer: Derek Angus
- Confirmation of member organisations – *ongoing and growing…!*
- Draft constitution drawn up and circulated to members for consultation

InFACT emerging activities

- Pandemic research preparedness

Pandemic research preparedness

- 3-day colloquium, June 2011
- Joint InFACT/LKSKI/ISARIC meeting
- Goal to create necessary global infrastructure to initiate clinical research in acutely ill patients rapidly and rigorously in response to future pandemic threats
- 100 international clinical investigators
- Funded by CIHR and PHA Canada
- Overview paper outlining a model for expedited pandemic research to be prepared/circulated/published

InFACT emerging activities

- Pandemic research preparedness colloquium
  - Perpetual, adaptive, global RCT

Perpetual, adaptive, global RCT (i)

- One of the conclusions of the colloquium was:
  - effective RCTs hard, if not impossible, to conduct if launched de novo during an epidemic/pandemic
  - far more lives lost from endemic severe acute respiratory infections than from pandemics
  - InFACT (with ISARIC) provides an opportunity to bring together existing/new groups, working globally, dedicated to RCTs in both intensive care and infectious diseases
  - such collaboration, to be successful, should follow a model for open access from concept to publication

Perpetual, adaptive, global RCT (ii)

- Discussion focused on borrowing from novel designs in oncology/psychiatry that allow:
  - on-going enrolment into multiple arms
  - flexibility regarding treatment options available at different time-points/care settings
  - flexibility regarding sample size and termination/initiation of new arms allowing transition to new questions as existing ones answered
- Next step - flesh out detail
  - workshop of trialists (December 2011) to generate draft potential study design for consideration by all InFACT member groups

InFACT emerging activities

- Pandemic preparedness colloquium
  - Perpetual, adaptive, global RCT
  - Pandemic/'flu registries group

Pandemic/'flu registries group

- Build on 2009/10 H1N1 pandemic collaborations
- Prepare for collection/management of data for any future global health emergency
- Linking with other relevant groups
- Establish infrastructure and relationships to allow:
  - development of dataset/data collection
  - principles/process for pooling/sharing data
- Chaired by Rob Fowler and Guillermo Dominguez-Cherit

InFACT emerging activities

- Pandemic preparedness colloquium
  - Perpetual, adaptive, global RCT
  - Pandemic/'flu registries group
  - Biology of severe influenza

Biology of severe influenza

- Build on 2009/10 H1N1 pandemic collaborations
- International severe influenza genetics program being developed:
  - To establish a network
  - To identify and engage critical care units
  - To identify genetic loci associated with susceptibility to SARI resulting from influenza
  - To establish a bioresource of DNA from cases of life-threatening SARI and unaffected controls.
  - To describe the epidemiology of SARI
- Led by Ken Baillie

InFACT emerging activities

- Pandemic preparedness colloquium
  - Perpetual, adaptive, global RCT
  - Pandemic/'flu registries group
  - Biology of severe influenza
  - Global capacity study

Global capacity study

- Aim to identify and create a registry of critical care units worldwide and understand capacity for care delivery and for research
- Simple, short questionnaire in development – please respond and not delete…!
- Challenges around:
  - contact/communication
  - translation
  - data ownership/access
- Led by Charles Gomersall (gomersall@cuhk.edu.hk)

InFACT emerging activities

- Pandemic preparedness colloquium
  - Perpetual, adaptive, global RCT
  - Pandemic/'flu registries group
  - Biology of severe influenza
  - Global capacity study
  - Building global collaboration

Building global collaboration

- Aim to address the significant challenges of building global collaboration and co-operation
- To provide a bridge between established member research groups and newer, or less well established, research groups to increase the capability of the latter
- To foster the creation of new research groups in regions without them
- Chaired by Steve Webb

InFACT emerging activities

- Pandemic preparedness colloquium
  - Perpetual, adaptive, global RCT
  - Pandemic/'flu registries group
  - Biology of severe influenza
  - Global capacity study
  - Building global collaboration
- Global supply/demand for acute care services

ACCESS (Accounting of Cities' Capacity for Emergency ServiceS) study (i)

- Estimating global supply and demand for basic acute care services in urban settings
  - Investigating the capacity to manage acute community acquired medical conditions in urban settings around the world
  - Describing both the burden of illness and the availability of acute healthcare services in large cities (population >100,000)
- Led by Neill Adhikari, Hannah Wunsch, Srinivas Murthy

ACCESS (Accounting of Cities' Capacity for Emergency ServiceS) study (ii)

- Currently piloting questionnaire in six cities eliciting information on, publicly available:
  - hospitals
  - hospital beds
  - ICU beds
  - ambulances

InFACT emerging activities

- Pandemic preparedness colloquium
  - Perpetual, adaptive, global RCT
  - Pandemic/'flu registries group
  - Biology of severe influenza
  - Global capacity study
  - Building global collaboration
- Global supply/demand for acute care services
- Outcome measures

Outcome measures

- Aim to inform the development and dissemination of standardised measures/metrics for critical care research
- Learning from other similar endeavours
- Systematic review of “when to measure mortality” ongoing
- Developing Terms of Reference
- Meeting planned for 2012
- Chaired by John Marshall

InFACT emerging activities

- Pandemic preparedness colloquium
  - Perpetual, adaptive, global RCT
  - Pandemic/'flu registries
  - Biology of severe influenza
  - Global capacity
  - Global collaboration
- Global supply/demand for acute care services
- Outcome measures
- Registries/databases

Registries/databases (routine)

- Establish a network for existing registries/databases
- Provide support for newer registries/databases
- Explore standardisation and development of novel tools for data collection/management
- Explore possibilities for collaborative research – either new or through data pooling or shared analysis plans/results
- Explore possible integration of global research requirements into registries/databases
- Chaired by Kathy Rowan

InFACT challenges (i)

- Formal "organisation" from 1 January 2012
- Establishing the Council – proposed as:
  - Executive Committee
  - One representative from each member group
  - Chairs of Working Groups
- Engage member groups and mobilise participation
- Communications – how to keep all up-to-date
  - member groups
  - members of member groups
- Website development

InFACT challenges (ii)

- Establish InFACT as a viable organisation:
  - business planning
  - funding – currently no external financial support
- Establish active Working Groups producing outputs
- Establish regular InFACT meetings (possibly at Brussels, ESICM, WFSICCM)

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