The cure comes from within

Taking part in clinical research

Clinical Trials 101

A guide for people with Parkinson's disease and other movement disorders and their caregivers

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UHN Movement Disorders

Volunteers are Essential

Volunteers are essential for every study

Medical advancements depend on research participants

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Volunteers are Essential

- To get from the lab to the pharmacy a new treatment can take decades and well over a billion dollars
- Half of that time is spent in clinical trials
- Close to 85% of all trials are delayed due to volunteer recruitment difficulties
- A shocking 30% fail to recruit a single subject

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Volunteers are Essential

- Delays in finding participants, leads to a huge waste of resources, money and most importantly time
- Clinical trial recruitment remains a huge issue
- Why?
  - Potential participants are not informed

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WHAT IS A CLINICAL RESEARCH STUDY?

Two Types of Clinical Research Studies

Observational studies

- Clinicians follow a group of volunteers, monitoring various aspects of their health. No attempt is made to affect the outcome

Interventional trials

- Researchers assess the safety and efficacy of a new intervention

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Observational Studies

- Contribute to a growing wealth of data that informs the course of future treatments
- Examples of what is learned:
  - Disease frequency in a population
  - Disease risk factors
  - Patient outcomes over time
  - Etc.

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Observational Studies

- The study may be as simple as filling out a survey
- Some may ask you to complete a series of tests or exercises
  - Measure the progress of your motor symptoms
  - Measure your cognitive health
  - Over the course of months or years

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Interventional Trials

May include:

- A new drug
- A new treatment
- A medical device or procedure
- A change in behaviour
  - Exercise
  - Diet
  - Etc.

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Interventional Trials

Discovery
Development
Preclinical Testing
Clinical Trials

Discovery

Initial testing of many molecular compounds

Leads to a ***few*** promising ones chosen to move onto the next step

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Interventional Trials

Discovery
Development
Preclinical Testing
Clinical Trials

Development

Promising compounds are tested to determine:

- The drug's effectiveness on its own and compared to existing drugs
- The dosage required
- How the drug is metabolized and excreted
- The best route to administer the drug
- Potential side effects, etc.

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Interventional Trials

Discovery
Development
Preclinical Testing
Clinical Trials

Preclinical Testing

The drug is tested for toxicity

Testing in living organisms or animal testing must follow the strict regulations set out by Health Canada

When the safety of a drug is established it moves on to clinical trials

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Next Step

Clinical Trials

Protocols that outline criteria:

- Choosing participants
- Size and duration of the study
- Dosage and method of administering the drug (treatment)
- How data is collected, reviewed, analyzed

- A robust and reliable study that will stand up to the scrutiny of the scientific community

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Clinical trials are conducted in four phases

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Clinical Trials – Phase 1

- Tested for the first time on humans
- Establish safety
- Identify side effects and how drugs react in human subjects
- Small in terms of numbers of volunteers
- Usually conducted on healthy human subjects

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Clinical Trials – Phase 2

- Larger, several hundred participants
- Tested to see how it works on specific diseases or conditions
- Further assess safety and effectiveness
- It is usually tested against a placebo

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Clinical Trials – Phase 3

- Larger still (several hundred to several thousand participants)
- Usually conducted at multiple centres
- Gather further data on the therapy's effectiveness, safety and side effects profile
- Compare to the standard treatments already available

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Clinical Trials – Phase 4

- Takes place after a treatment has Health Canada approval
- Looks at long-term side effects and effectiveness with widespread use in the marketplace
- Health Canada may at any point:
  - Put additional warnings or cautions on a drug's use
  - Change the prescribing recommendations
  - If new safety concerns arise, take it off the market

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BEHIND THE SCENES *of a* CLINICAL DRUG TRIAL:

PHASE 1

Tested on a small group to assess safety, dosage, and identify side effects

PHASE 2

Usually tested on 100+ people to learn how it works on specific diseases or conditions

PHASE 3

Usually tested on 1,000+ people to compare it to commonly used treatments

PHASE 4

Trials after drug is approved to learn best way to use it, long-term benefits and risks

HealthyCanadians.gc.ca

Canada

Volunteers are Essential

Volunteers are essential for every study

Medical advancements depend on research participants

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Why participate?

- Active role in health care is empowering, and feels good
- Contribute to new medications and therapies
- May help future generations and others with the same disease
- Contribute to moving science forward
- Without patient volunteers, no clinical trials
- Without clinical trials, no cure

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What are the eligibility factors?

- Age and gender
- The type of disorder
- The length of time since diagnosis
- Treatments or drugs being taken
- Other medical conditions will be considered
- Eligibility criteria is often narrow in clinical trials to help ensure participants' safety
- The Study Coordinator will determine eligibility

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Potential Inconveniences and Risks

Clinical trials:

- May have side effects
  - The safety of participants is foremost but unforeseen issues may arise
- May have to stop or change your regular treatment protocol
  - The experimental meds may not be as effective
- No control whether over the placebo vs. the drug being studied
- Even if the study's treatment works, you may not have continued access to that treatment until it reaches the marketplace
- Significant time commitments and travel may be required
  - Expenditures and overall costs of participating in the trial may not be adequately covered

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Considerations

You should ***not*** participate:

- To get a new treatment
- To please your doctor
- If you are not properly informed of all aspects of the study
  - Including potential risks or side effects
- If you are not able to fulfil the study time and commitments
- If you are not willing to modify your lifestyle
  - For example, dietary changes or exercise regimes

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Informed Consent will be required

- Prior to beginning any study, the risks, potential benefits and alternatives must be reviewed in enough detail with you that you are able to give what is called “informed consent”

- By giving consent you are agreeing to participate with the suggested protocol but you may withdraw at any time if necessary

- Only once you are satisfied that your concerns have been addressed to your fullest satisfaction, should you give informed consent to participate

What should I know ?

Who should I ask ?

Before consenting to participate in a Clinical Research Study

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What to ask

- What kind of trial/study is it
- Why is it being done
- How will this research affect me
- How long is the study
- How many visits
- What are the benefits and risks
- What are my rights as a participant in the study

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Who to ask

- Your family doctor
- Your movement disorder specialist
- Any member of the clinical research team
  - The trial coordinator
  - Nurses, research assistants
- Other health care professionals
- A movement disorder patient with clinical research experience

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Are all Volunteers Movement Disorder Patients?

No. Caregivers & family members are encouraged to take part

- A healthy control is a person who does not have the disorder
- Results from healthy controls are compared to results from the patient group – critical to the outcome
- However, these individuals can be challenging to find

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Remember, you are a key member of the clinical research team

Without you there is no research

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Who do I contact about participating in a clinical research study

Research coordinators at UHN

Your movement disorder specialist

Other people with movement disorders (md/pd ambassadors)

mdcclinicaltrials@uhn.ca

What about COVID-19?

- Your safety is our priority.
- Your study team is carefully considering which visits are needed in-person, and which may be done by telephone or video conference.
- If the risk of COVID-19 changes, your study team will contact you if your visit schedule changes, or if it is best for you to stay home.
- Participation in research is always voluntary. You are not required to keep your appointment as a research participant.

What about COVID-19?

What can I expect when I come to the hospital?

- **Entrance Screening**

UHN screening staff are at each entrance. Please answer their questions honestly.

- **Universal Masking**

Everyone entering UHN must wear a mask. You will be given a mask by screening staff at the hospital entrance. You must wear your mask at all times while inside UHN.

- **Hand Hygiene**

You must wash your hands when you enter the hospital, and before and after putting on a mask. Wash your hands often throughout your visit.

- **Physical distancing**

Please practice physical distancing inside the hospital. Follow directions from staff, wall signage and floor markers.

- **No visitor policy**

Only one **Essential Care Partner** who is part of your "safe social circle" will be allowed to accompany you, and only if it is essential.

What about COVID-19?

Online Screening Tool for Patients

1. When you arrive at the hospital, go to uhnpatientscreen.ca on your mobile device.

2. Answer the questions about COVID-19 symptoms, close contact, and recent travel.

3. Show your final screen to the entrance screening staff. This screen will have a date, time and either say PASS, or will ask you to speak further with staff.

What about COVID-19?

Information at UHN

https://www.uhn.ca/Covid19#inside

Information for Research Participants

https://www.uhn.ca/Covid19/Pages/COVID_research_participants_updates.aspx

Key recent clinical trials at MDC: Parkinson's disease

- **MDS Clinical Diagnostic Criteria for Parkinson's Disease:** Demonstrated new diagnostic criteria able to more accurately diagnose Parkinson's disease. 60 MDC patients involved.
- **Apomorphine sublingual film:** to **p**rovide an efficacious, on-demand treatment for ***off episodes*** for most patients with Parkinson's disease in this trial
- **SPARK study:** to assess the safety, pharmacokinetics and pharmacodynamics of an alpha-synuclein antibody in early PD. https://www.thesparkstudy.com/en-us/alpha-synuclein.html

Key recent clinical trials at MDC: Parkinson's disease

- **Safinamide** "The outcomes of this trial support safinamide as an effective adjunct to levodopa in patients with PD and motor fluctuations to improve on time without troublesome dyskinesia and reduce wearing off" (JAMA Neurology 2017).

- **CVT-301 (levodopa inhalation powder)** improved motor scores of patients with Parkinson's disease during off-periods, with few severe or serious side effects, leading to FDA drug approval in the U.S. (Lancet Neurology 2019)

Key recent clinical trials at MDC:

DBS and Ataxia

DBS: Levodopa Vs. Dopamine Agonist after Subthalamic Stimulation in Parkinson Disease. Funded by the Michael J. Fox foundation, provides generated evidence on how to simplify pharmacological treatment after functional neurosurgery for Parkinson's disease.

- **Self-Adjustment of Deep Brain Stimulation Delays Optimization in Parkinson's disease.** Use of a remote control by patients was associated with a higher number of side effects,
- Highlighting the need for other methods for faster and safer stimulation programming.

Ataxia: SCA3 Facial Movement Disorders Study: to better characterize facial movement abnormalities and clinicians' ability to accurately identify these movements.

Testimonials

"Parkinson's research studies are something that I can do uniquely well, since I have Parkinson's. Participating in such studies makes me feel less like a victim and more like an active and energized person who is fighting Parkinson's."
– **Bart Narter,** Parkinson's Ambassador Davis Phinney Foundation

"First off, you will get a Parkinson's screening at each test; so, you get regular feedback on how your Parkinson's is progressing. Second, you are helping to find the cure! Third, you may get little cures for yourself, as I have experienced a couple of times. Finally, living well equals living cool, and as a result of these trials I get exposed to and in many cases I get to work with very cool, state-of-the-art medicine."
– **Joe O'Connor,** Parkinson's Ambassador Davis Phinney Foundation

Testimonials from MDC patients

"When I was diagnosed in 2010 I went in search of a second opinion. Luckily I was able to get an appointment at MDC where Dr. Lang confirmed the diagnosis. I wasn't taken on as a patient but was asked about taking part in clinical trials. I of course said I would like to take part in any study going. As part of these studies I was at MDC many times and had more than regular check ups. Eventually it just seemed to make sense that I continue at MDC as a patient of Dr. Lang's. Taking part in the studies brought me into contact with many different movement disorder specialists, each with their own unique approach and perspective. It was a great learning experience"

– **Gord Myers,** Parkinson's Ambassador Patient Advisory Board

"Without volunteers clinical trials can't move forward. The ideas that have been nurtured and developed over many years by scientists need the help of volunteers to take the next step to become a reality. To change lives for the better. To change my life and yours. We all want a cure, and that would be amazing, but along the way our quality of life improves, just a bit, with the help of research completed at TWH MDC. Choose to participate in the process of making life with a movement disorder better.

"MDC staff were all great. They were always professional and ready to answer any questions I might have. I felt at ease in their hands."

– Gord Myers, Parkinson's Ambassador Patient Advisory Board

"I would greatly encourage people with a diagnosis of Parkinson's to take advantage of any opportunity to participate in any and all available clinical trials for which they are eligible! They may well experience individual benefit; Study participants will have access to the latest treatments, some of which are accessible only to study participants; Study participants are seen by a Movement Disorder Neurologist on a regular and more frequent basis than would be the case with their own physicians; and there is the altruistic motivation- to make a contribution for people with Parkinson's in the future and to make a contribution to medical science.

"I have found it interesting and informative being a study subject. I have learned about the newest and most innovative research into the treatment of Parkinson's."

– Janice Duff, Current Parkinson's Clinical Trials Participant,
Previous Study Coordinator for 10 years and Clinical Monitor for Parkinson's.

Learn more about clinical research at the MDC

PARKINSON'S DISEASE STUDIES					
Study Name	Study Focus	Study Procedures	Frequency/Duration	Special Requirements	Recruitment
Pharma 2B	Early treatment for PD (No placebo)	Questionnaires Blood samples	7 visits 3 hours 3.5 months	35-80 years old Early untreated PD Diagnosis less than 3 years	mdcclinicltrials@uhn.ca
Theravance 0169	Treatment for bothersome hypotension	Tilt table Blood samples Questionnaires Neurological assessments	4 visits 4 hours 3 months	PD or MSA with snOH Orthostatic hypotension meds tapered off for 7 days (if applicable)	mdcclinicltrials@uhn.ca
Neuraly Inc.	Early treatment with NLY01 (approved for diabetes).	Questionnaires Clinical assessments Blood samples 36 total injections	52 weeks Visits every 4 weeks	30-80 years old with early PD who are not receiving dopaminergic treatment.	mdcclinicltrials@uhn.ca

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Learn more about clinical research at the MDC

PARKINSON'S DISEASE STUDIES					
Study Name	Study Focus	Study Procedures	Frequency/Duration	Special Requirements	Recruitment
Cannabis oil	Cannabis oil for pain in PD	Questionnaires Clinical assessments Blood samples	5 visits over 6 weeks	Parkinson's Patients with Bothersome Pain	mdcclinicltrials@uhn.ca
Tempo-01	New DA (D1 & D5 receptor)	Questionnaires Clinical assessments Blood samples ECG	27 weeks, clinic visit every 4 weeks	40-80 years old. 3<diagnosis, untreated PD	mdcclinicltrials@uhn.ca
ROPAD	Test for LRRK2 and GBA mutations (also 68 PD panel and Whole Genome Sequencing)	Blood sample Clinical assessments	1 visit	220 participants: PD patients Family members of LRRK2 positive. Healthy participants from high risk population.	mdcclinicltrials@uhn.ca

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PARKINSON'S DISEASE STUDIES					
Study Name	Study Focus	Study Procedures	Frequency/Duration	Special Requirements	Recruitment
LRRK2	LRRK2 Biomarkers	Eye Tracking Blood samples Actigraphy	5 visits over 6 weeks	Must have LRRK2 mutation No DBS 10 PD patients 40 Healthy controls	mdcclinicltrials@uhn.ca
LRRK2 Genetic Registry	Gene mutations	Creating a directory of PD patients with gene mutations	Future research	Gene mutations causing PD	mdcclinicltrials@uhn.ca
CCNA	Cognitive impairment	Biospecimens MRI Questionnaires Assessments	4 visits 4-5 hours 2 year follow up study	50-90 years old Requires study partner Parkinson's MCI/Dementia or Lewy Body Dementia diagnosis	mdcclinicltrials@uhn.ca

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PARKINSON'S DISEASE STUDIES					
Study Name	Study Focus	Study Procedures	Frequency/Duration	Special Requirements	Recruitment
BEAM	**Brain amyloid and neurodegeneration**	PET Blood samples KEI Retina MRI	4 visits 4-5 hours 3 months	50-90 years old Requires study partner Parkinson's MCI/Dementia or Lewy Body Dementia diagnosis	mdcclinicltrials@uhn.ca
FOG	Brain mechanisms of walking for PD patients	Walk through Virtual Reality (involves EEG & MRI)	1-4 visits 4 hours 3 months	Mild to moderate PD with or without freezing of gait No PD meds for 12 hrs No pacemaker	mdcclinicltrials@uhn.ca
Pathophysiology of PD	Changes in brain functions	TMS Brain Stimulation EEG	1-4 visits 4 hours 3 months	Mild to moderate PD with STN DBS. No Amantadine for 12 hours (if applicable) DBS turned off for a portion of the visit	mdcclinicltrials@uhn.ca

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Learn more about clinical research at the MDC

ATYPICAL PARKINSONISM (PSP/MSA/CBD/LBD) STUDIES					
Study Name	Study Focus	Study Procedures	Frequency/Duration	Special Requirements	Recruitment
Imaging in Parkinsonisms	PET study	PET MRI Clinical Assessments	1 visit 6 hours	40-80 years old PSP/MSA/CBD movement disorders No pacemaker No claustrophobia	mdcclinicltrials@uhn.ca
alpha-Synuclein	Biomarkers in PD	Lumbar puncture Skin biopsy Blood and saliva Questionnaires	1-2 visits	25 pts early untreated PD < 2 yrs 25 advanced PD pts 25 MSA or PSP pts 20 RBD pts 25 controls	mdcclinicltrials@uhn.ca
Theravance 0169	Treatment for bothersome hypotension	Tilt table Blood samples Questionnaires Neurological assessments	4 visits 4 hours 3 months	PD or MSA with snOH Orthostatic hypotension meds tapered off for 7 days (if applicable)	mdcclinicltrials@uhn.ca

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DYSTONIA STUDIES					
Study Name	Study Focus	Study Procedures	Frequency/Duration	Special Requirements	Recruitment
Writer's cramp	Cortical plasticity in Focal hand dystonia before and after botoxin injection	TMS Brain Stimulation Writing assessment	4 visits 4 hours 3 months	Right hand writer's cramp diagnosis. Receiving benefit from botoxin injection	mdcclinicltrials@uhn.ca
Musician's Dystonia	Studying connections between the cerebellum and parts of the brain for musicians	TMS(cTBS) Brain Stimulation MRI	2 visits 2 hours 3 months	Right hand Musician's Dystonia diagnosis No pacemaker No claustrophobia	mdcclinicltrials@uhn.ca
Dystonia Coalition	Blood research bank	Blood Samples Questionnaires Videotaping	1 visit 1.5 hour	18+ years old with last botox 2+ months prior	mdcclinicltrials@uhn.ca

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Other resources for finding clinical trials:

Clinicaltrials.gov
https://clinicaltrials.gov/

Michael J. Fox Trial Finder
https://www.michaeljfox.org/trial-finder

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Thank you