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**CaHRU and LIH Improvement Science and Research  
Methods seminar**

**Researching rare diseases**

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# Rare diseases

- Rare disease defined by EU as life-threatening or chronically debilitating disease affecting  $\leq 5$  in 10,000 and requiring special efforts for effective treatment
- Between 6,000 to 8,000 known rare diseases and around five new rare diseases per week described in medical literature
- 1 in 17 people (6%) affected by rare disease during lifetime
- Approximately 3.5M in UK and 30M across Europe
- Significant cause of illness requiring resources and capacity of NHS and other care services

# Why research rare diseases?

- Rare diseases (together) affect a large number of UK population
- Under-researched
- More research needed on most effective approaches for delivering care for most rare diseases
- Call for research into rare diseases (UK Health Departments consultation, 2012)
- Illuminating the Rare Reality (2019) Report, Recommendation 5: ‘Protect and enhance the UK’s role in rare disease research. Ensure capacity for, and commitment to, research into rare diseases is not diminished and that the UK continues to attract investment’
- A Recommendation of the Council of the European Union (2009) called for each EU State to have in place a rare diseases plan or strategy by the end of 2013



# UK strategy for rare diseases

- UK Strategy for Rare Diseases published in 2013
- Aim of Strategy is to ‘ensure no one gets left behind just because they have a rare disease’
- One key feature of the strategy was ‘building on research to improve personalised approaches to healthcare for those with a rare disease’
- Minister for Rare Diseases, Nicola Blackwood



# Guillain-Barré Syndrome (GBS)

- Immune-mediated polyradiculoneuropathy, annual incidence 1/91,000 - 1/55,000
- All ages; male: female 1.5: 1
- First phase (few weeks): rapidly progressive muscle weakness and/or acute paralysis; sensory disturbances, intense pains and cramps; often acute respiratory failure, 20-30% of need mechanical ventilation
- Second phase (variable duration): symptoms become stable; other manifestations (cardiac arrhythmias, hyper/hypotension and gastric dysmotility) may occur
- Third (recovery) phase (few months or longer): symptoms slowly regress; many have residual findings (weakness, sensory disturbances, fatigue or pain) for many months or even years
- Variable prognosis: around 50% of patients recover completely or have only minor sequelae, 20% are unable to walk after 6 months, and 3% die

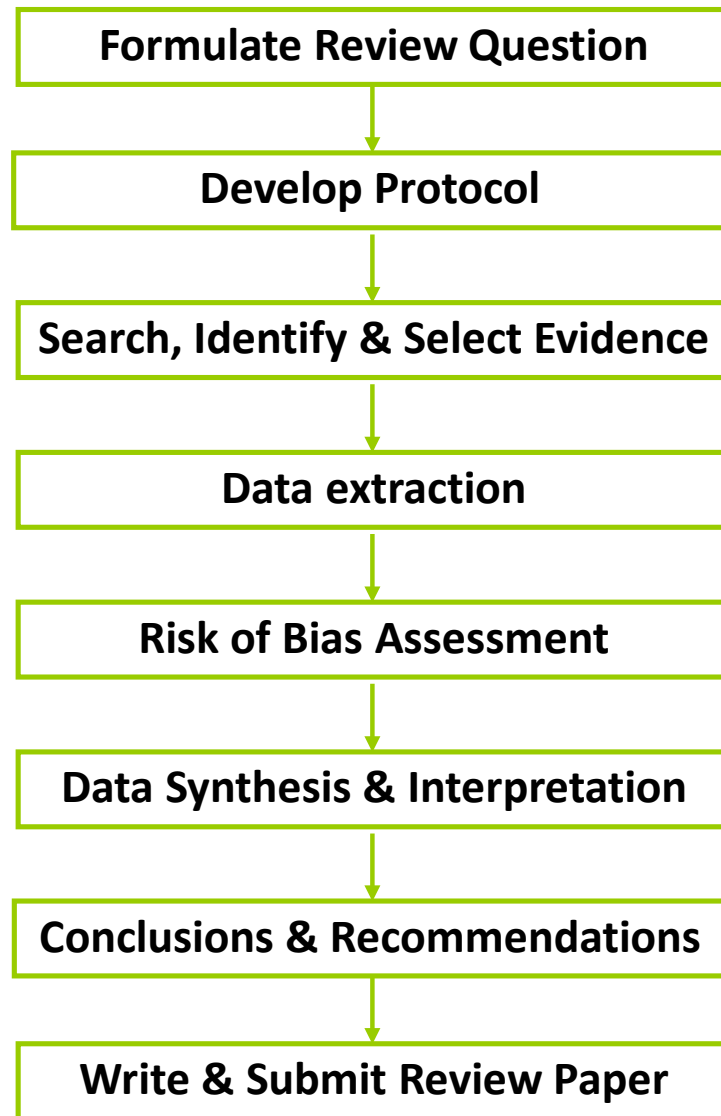


# Our approach to researching GBS

Complex mixed methods design:

- **Systematic review and metasynthesis:** To review patients' experiences of GBS at diagnosis, discharge and during recovery by conducting a systematic review and thematic meta-synthesis of qualitative studies of patients' experiences of GBS
- **Qualitative:** To explore experiences particularly focussing on the period post-discharge from hospital and return to the community, of people living in the United Kingdom and Republic of Ireland who have had GBS, from physical, psychological and social, including occupational, perspectives using qualitative interviews to understand health and social care needs, facilitators and barriers to recovery and return to function
- **Quantitative:** To develop, validate and administer a questionnaire survey to elicit the range of experiences, health and social care needs, and facilitators and barriers to recovery and return to function of people with GBS, resident in the UK and Republic of Ireland.

## Key stages in conducting our systematic review



# Our review question

PICo

- Population
- Phenomena of Interest
- Context



What are **patients'** experiences and perceptions of GBS and its variants at diagnosis, discharge and during recovery?

Population

Phenomena of Interest

Context

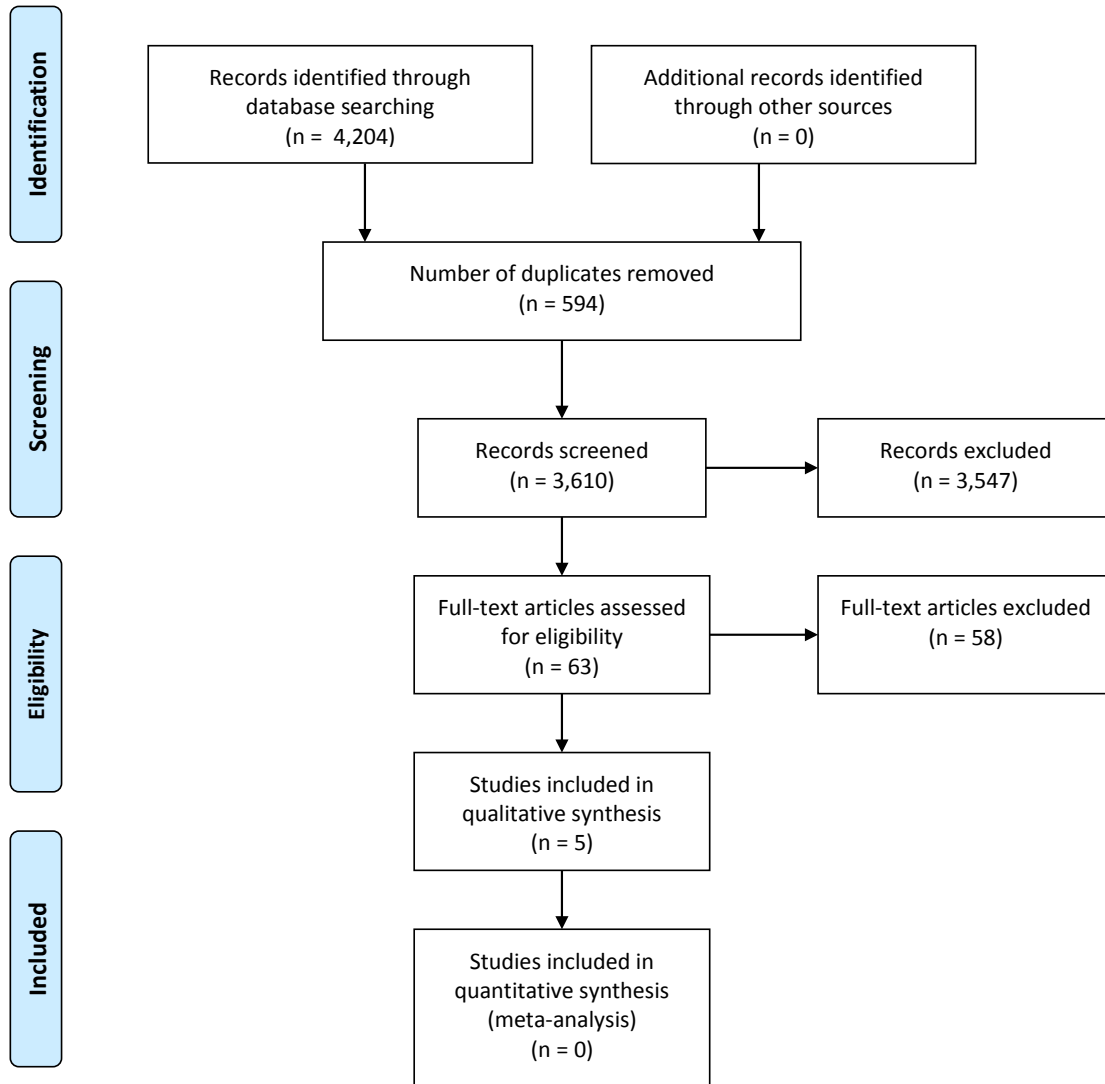


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## PRISMA 2009 Flow Diagram



# Main study characteristics

- Published between 2003 and 2015 (Australia, Sweden, UK, and, USA).
- One study was a PhD thesis.
- People living with GBS only (no other variants, such as CIDP or Miller-Fisher syndrome).
- Both men and women, but more male participants overall (55/94).
- Participants' ages ranged from 16 to 80 years.
- Individual semi-structured interviews only; none included focus groups.
- Majority focused on the overall experiences of people during hospital care or recovering from GBS; one study focused specifically on their experiences of returning to work following recovery from GBS.



# Risk of bias assessment

**Table 3. Critical appraisal/quality assessment of studies**

Study	CASP01	CASP02	CASP03	CASP04	CASP05	CASP06	CASP07	CASP08	CASP09	CASP010
Cooke & Orb, 2003	●	●	●	●	●	●	●	●	●	●
Forsberg et al., 2008	●	●	●	●	●	●	●	●	●	●
Forsberg et al., 2015	●	●	●	●	●	●	●	●	●	●
Hooks, 2015	●	●	●	●	●	●	●	●	●	●
Royal et al., 2009	●	●	●	●	●	●	●	●	●	●



# Data synthesis & interpretation

- We used thematic synthesis, following the Thomas and Harden (2008) approach.
- Six themes:
  - From uncertainty to hope;
  - Feeling lost in a changing life;
  - Fractured care;
  - Positivity towards recovery;
  - Adjustment;
  - Towards a new self.



# Theme 1: From uncertainty to hope

- Initial strange sensations;
- Rationalising symptoms & misattributing diagnosis;
- Participants' eagerness to find out what's happening to them;
- Uncertainty;
- **Healthcare professionals' lack of knowledge and experience with GBS;**
- Need for information about GBS;
- Prospect of a positive prognosis;
- Hope of recovery.

“I just wish that, um, that the people who were treating me had known more about it, You know, it's not comforting when, you know, a nurse walks in and said: I didn't know anything about it, so I had to Google it. You know, I didn't find that comforting. And there were – there was more than one person that – that said they had never really heard of it.”



## Theme 2: Feeling lost in a changing life

- Experience of physical symptoms;
- Loss of identity;
- Dependency, vulnerability and feelings of helplessness;
- Feelings of shame and embarrassment;
- **Psychological responses to GBS;**
- Effects of GBS on family life;
- Difficulties with re-assuming social lives;
- Experiencing work-related difficulties.

“There were so many [emotions]. Frustration that I couldn’t figure out what was wrong with me. Guilt because I was taking so many drugs. There was...a not knowing what was wrong with me was, um, just heart-breaking. A frustration when I fell at work, I laid in the doorway of my job, and I just cried.”



## Theme 3: Fractured care

- Lack of continuity of care;
- Lack of person-centred care at hospital;
- Feeling not listened to by healthcare staff;
- Communication issues with healthcare staff;
- **Feeling that needs are not being met by healthcare staff;**
- Lack of publicity about GBS.

“I remember one day they had me riding on a bicycle... [and] a physical therapists [should] not push, push, pushing somebody to the point of exhaustion....I just think it's set up for a different kind of rehab than what I needed”



## Theme 4: Positivity towards recovery

- Positive feelings towards healthcare received (e.g. physical care needs were met; kind staff; medical staff were conscientious);
- Getting support from family and friends (including colleagues);
- Importance of peer support;
- **Maintaining a positive attitude.**

“Your life isn’t over. And I know it seems like it but it’s not. It’s going to get better but your attitude is everything. Your attitude will make or break this thing for you”





# Theme 5: Adjustment

- Experiences of recovery varied;
- Symptom management;
- Need for control and independence;
- **Achieving milestones;**
- Acceptance of their situation;
- Remaining positive, despite persisting symptoms.

“Well, little by little, you know things got better. I mean, I can remember being so excited at home when I had to – I could actually get myself a cup of coffee and walk across the room without a walker...with a cane...and sit down in a chair, and do that all by myself. I thought that was just ...a major feat.”



## Theme 6: Towards a new self

- Desire to go back to 'normal' pre-GBS selves;
- Hiding GBS;
- Fear of stigma;
- Others' perceptions of GBS;
- **Returning to work seen as going back to 'normal' self;**
- Motivations for going back to work;
- Facilitators and barriers to going back to work;
- Re-evaluating life.

“That [work] was good for me because I was normal again, I thought I was the same as I was before I had the Guillain-Barré, I was the same person again. Obviously I wasn't but I thought I was, and that was good enough for me”



# Systematic review conclusions

- Exploring this literature has enabled us to:
  - Identify how patients may need extra support to cope better with their recovery;
  - Identify ways that healthcare professionals and services can help facilitate further such a recovery;
  - Inform the qualitative study on patients' experiences of GBS.
- One of the most important areas that needs to be addressed is the lack of knowledge about GBS among the majority of healthcare professionals.
- One factor that positively influenced management and eventually outcomes was having a positive attitude and thinking towards recovery.
- Being diagnosed with and surviving GBS was a life-changing experience for all participants.



# Qualitative study

**Aim:** To explore experiences of people with GBS: physical, psychological, social and occupational perspectives.

## **Methods:**

- University ethics approval
- Purposive sample of 16 participants recruited using Flyers on GAIN website/Facebook
- Individual face-to-face and telephone interviews
- Thematic analysis facilitated by Nvivo 11.



# Characteristics of participants

<i>Participant details</i>	<i>No of participants</i>	
<i>Location</i>	North	12
	South	5
	Northern Ireland	1
	North Wales	1
<i>Age</i>	30-39	4
	40-59	7
	60-79	5
<i>Sex</i>	M	9
	F	7
<i>Ethnicity</i>	White	15
	(Black, Asian and minority ethnic (BAME))	1
<i>Marital status</i>	Married/cohabitating	12
	Single/separated/divorced/widowed	4
<i>GBS variant</i>	GBS	6
	GBS variant ( AIDP, AMAN, AMSAN, Miller Fisher)	7
	Not known	3



## Findings - 6 key themes

- Importance of early diagnosis
- Experiences of inpatient care
- Active support for recovery
- Communication
- Awareness, knowledge and information provision
- Redefining recovery.

<p>Importance of early diagnosis</p>	<p>“There is no doubt, if the GP hadn’t got it spot on first time, then I would have ended up in intensive care. It is only through that early diagnosis, that they were able to start treatment that much quicker” (Participant[P]7).</p>
<p>Experience of inpatient care</p>	<p>“In the intensive care unit, there was a wonderful nurse. She was absolutely fantastic...; but some other nurses where not as nice at all; very unpleasant” (P1).</p>

# Active support for recovery

Healthcare factors that helped or hindered recovery	
Early & correct investigations	“I got nerve conduction tests; had a lumber puncture...that night” (P4).
Adverse effects of treatment	“I am not sure whether it was during or after the treatment, but I started getting an allergic reaction on my hands” (P15).
Disease factors that helped or hindered recovery	
Being fit and active	“I was really fit. That may help. I was running, doing spin classes; really fit” (P7).
Residual physical <u>problems</u>	“I still have peripheral neuropathy and my memory is just shot. I suffer with chronic fatigue as well” (P1).



## Psychological factors that helped/hindered recovery

Being positive	“Positive mental attitude. If your glass is always half empty, you are going to suffer terribly” (P3).
Residual psychological effects	“I still get night terrors. Basically my partner just has to hold me; and I am screaming in my sleep” (P1).

## Social factors that helped or hindered recovery

Peer support	“You need role model. I now volunteer through the GAIN charity. I go into hospitals and I visit people” (P6).
Stigma of disability	“I didn’t like to be seen as disabled. I didn’t like that label put on me” (P4).

## Occupational factors that helped or hindered recovery

Supportive employer

“My company was extremely supportive. They gave me little bits of work back at a time. I wasn’t stressed or loaded on” (P11).

Unable to work

“I haven’t been to work ever since it happened. I was working for myself” (P3).

Communication	“I think communication, when you can’t speak, is really difficult, incredibly frustrating. You couldn’t tell people when you were in pain or wanted to go to the toilet” (P1).
Awareness, knowledge and information provision	“It is the awareness that needs to happen. I see about it every day because I follow it all on Facebook, but if there weren’t any social media, even less people would know about it” (P2).
Redefining recovery	“It is very important to accept that you have GBS, and your recovery maybe slow, just having to accept the change in your life” (P11).

# Qualitative study conclusions

The findings provide a framework to:

- Understand the factors that helped or hindered participants' journey from symptom onset to recovery
- Understand the care and support/needs of GBS patients
- Inform the survey.

# Questionnaire survey

- Online using Qualtrics
- Piloted with a small group of interviewees
- Revised in line with comments and suggestions
- 291 responses over 6 weeks

# Responder characteristics

Characteristic		N = 291	(%)
Country	UK	249	(85.6)
	Ireland	4	(1.4)
Sex	Female	130	(44.7)
	Male	140	(48.1)
Age	<18	2	(0.7)
	19-39	40	(13.7)
	40-59	96	(33.0)
	60-79	123	(42.3)
	80+	9	(3.1)
Ethnicity	White	264	(90.7)
	BAME	5	(1.7)
Marital	Single	5	(19.6)
	Married	168	(57.7)
	Other	45	(15.4)

# Diagnosis, year and time to present

Characteristic		N = 291	(%)
<b>Condition</b>	Guillain-Barré	202	(69.4)
	CIDP	46	(15.8)
	Other	22	(7.6)
<b>Year diagnosed</b>	2015-2019	116	(39.9)
	2010-2014	54	(18.6)
	2005-2009	33	(11.3)
	2000-2004	18	(6.2)
	Before 2000	49	(6.8)
<b>Time to presentation</b>	1-3 days	158	(54.3)
	4-6 days	40	(13.7)
	7-9 days	19	(6.5)
	10-14 days	14	(4.8)
	15-28 days	11	(3.8)
	>28 days	20	(6.9)

# Place, time and consultations to diagnosis

Characteristic		N = 291	(%)
First medical help	GP	163	(56.0)
	ED	67	(23.0)
	Other	32	(11.0)
Time to diagnosis	1-7 days	161	(55.3)
	8-14 days	31	(10.7)
	15-28 days	28	(9.6)
	>28 days	41	(14.1)
Consults to diagnosis	1	106	(36.4)
	>1	148	(50.9)

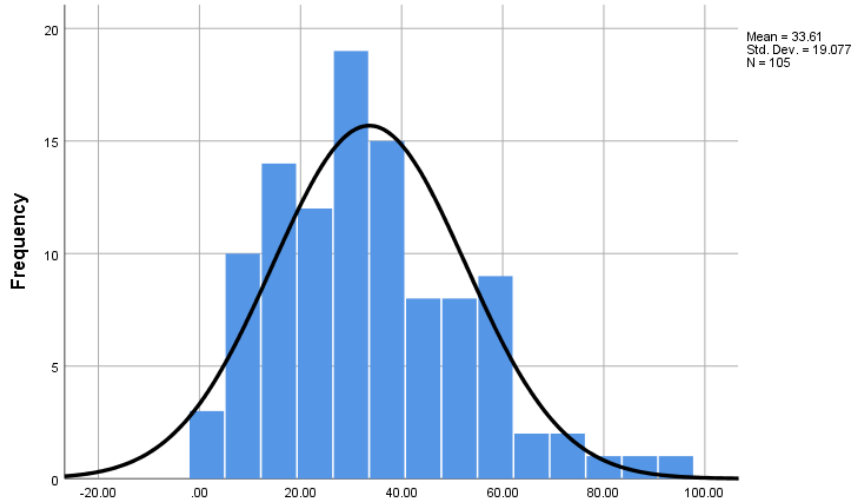


## Other diagnoses

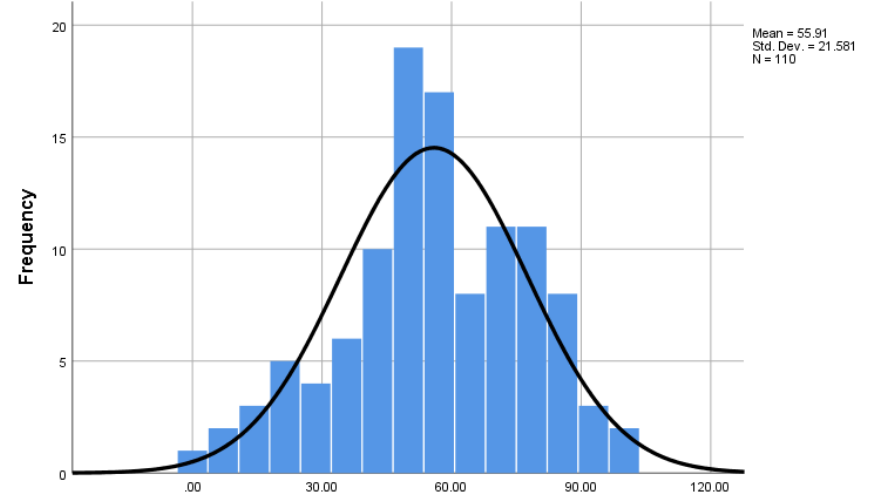
- 'Bug', 'flu, virus, ear infection, urinary infection, encephalitis
- Stroke, MS, MND, migraine, carpal tunnel syndrome
- Fibromyalgia, chronic fatigue syndrome, spinal fracture, disc
- Diabetes, high blood glucose, high blood pressure
- Anxiety, depression, stress, hyperventilation
- Pregnancy-related, Raynaud's, botulism

# Symptom severity during illness

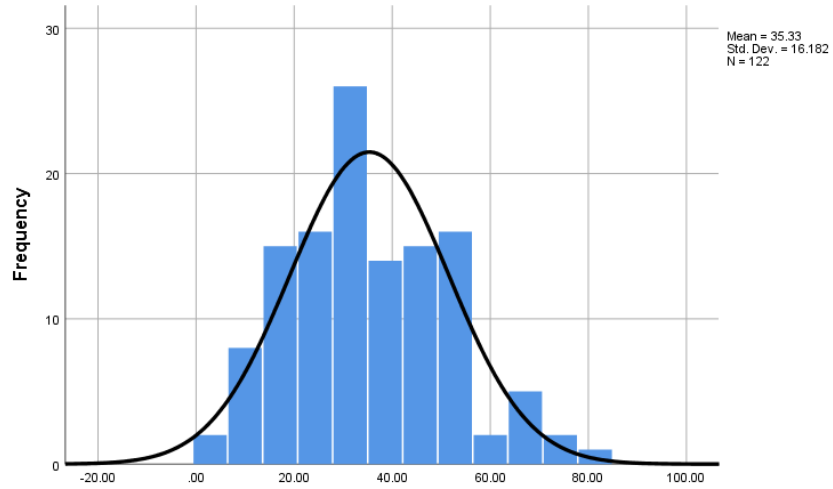
SEEKHELPSYMP TOM score



DURINGILLNESSSYMP TOM score

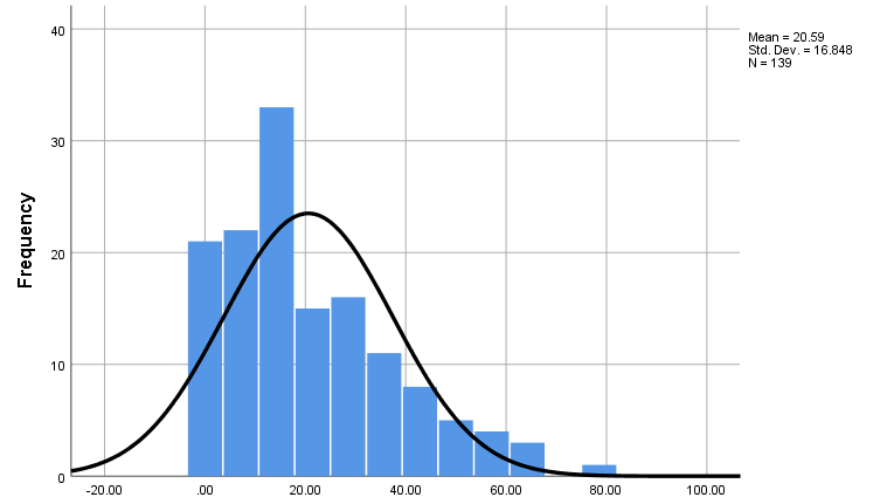


RESIDUALSYMP TOM score



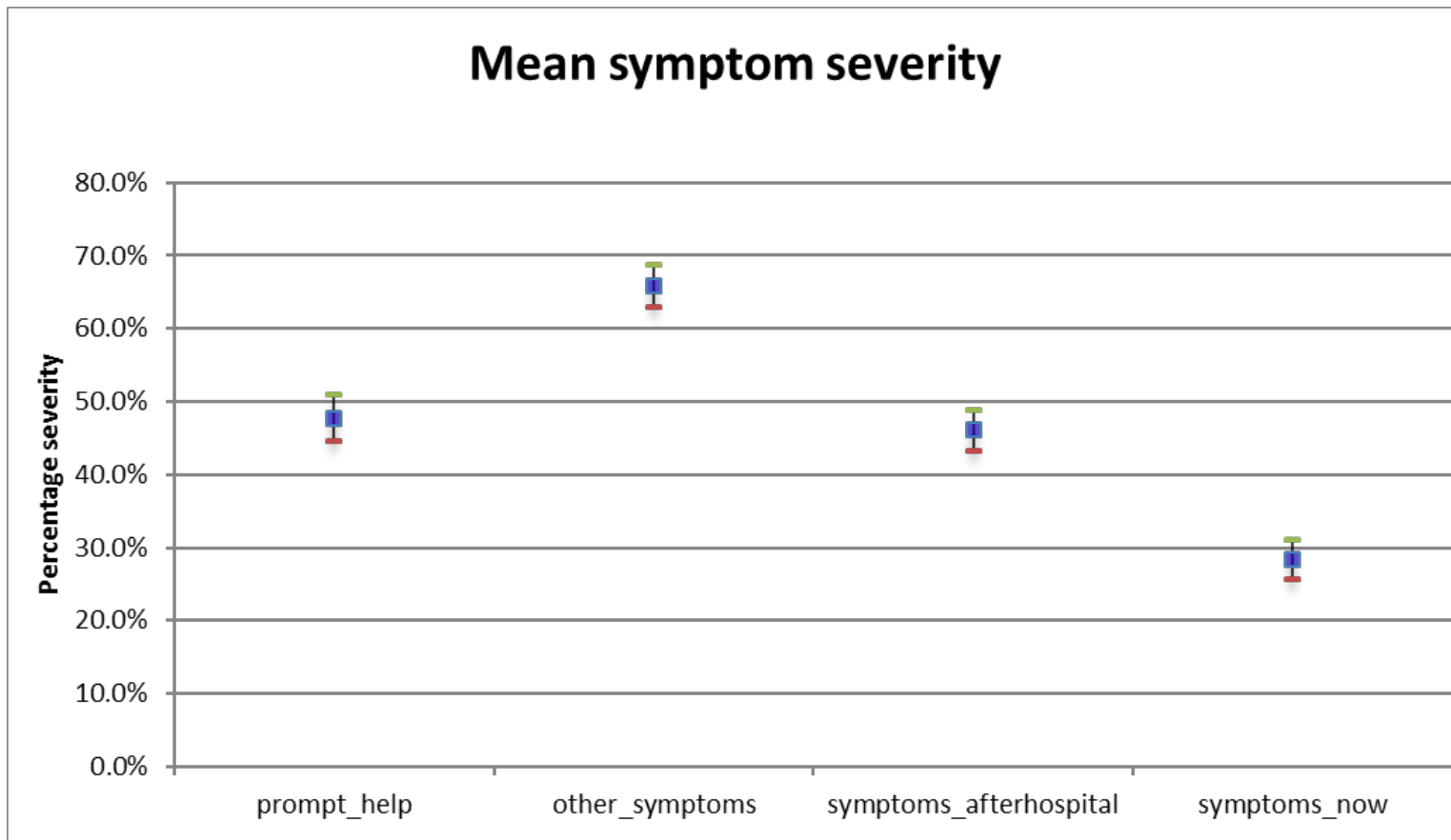
RESIDUALSYMP TOM score

CURRENTSYMP TOM score

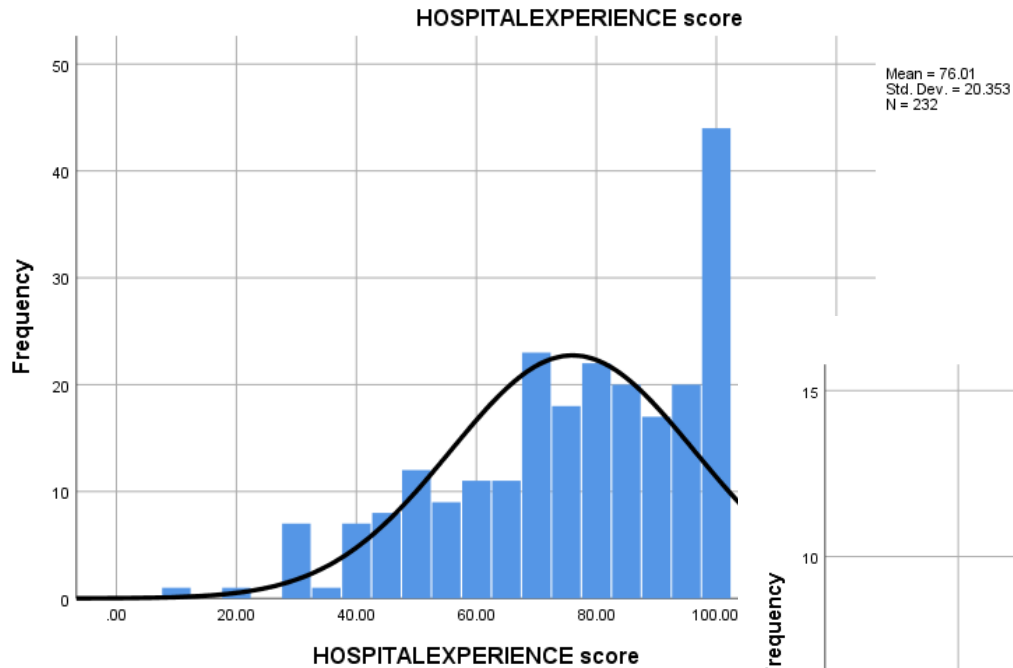


CURRENTSYMP TOM score

# Mean symptom severity at onset, hospital, discharge and current



# Experience during hospital and follow-up



## Information preference

Source	Number = 291	(%)
Health care staff	202	(69.4)
Charities, e.g. GAIN	173	(59.5)
Patients via social media	99	(34.0)
Online	27	(9.3)

## Information rating

	Excellent	Very good	Fair	Poor	Very poor
Health care	25 (8.6)	66 (22.7)	67 (23.0)	31 (10.7)	27 (9.3)
Charities	96 (33.0)	81 (27.8)	17 (5.8)	4 (1.4)	5 (1.7)
Social media	31 (10.7)	60 (20.6)	41 (14.1)	3 (1.0)	4 (1.4)
Online	15 (5.2)	33 (11.3)	22 (7.6)	-	3 (1.0)

# Factors associated with symptom improvement

Ordinal regression model showing factors associated with improvement in symptoms

- Age: Younger  $\leq 39$  years
- Married
- Early presentation:  $< 7$  days
- Early diagnosis 1-7 days
- ICU (vs general ward)
- Immunoglobulins perceived as positively affecting recovery

# Conclusions

- Possible methods vary depending on funder requirements, clinical condition, previous research, knowledge gaps and agreed aims
- Use methods that involve existing data and accessing participants remotely if resources limited
- Work with a patient group, funder or charity helps to recruit participants
- Link with national experts in GBS



# References

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**Thank you for listening!**



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