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香港大學藥理及藥劑學系

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HARVARD MEDICAL SCHOOL AFFILIATE

Tips on writing grant proposal on Advanced Medical Research

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HKU Med

Conflict of interest

I receive research support from:

1. Amgen
2. MSD
3. Zuellig
4. Roche
5. Sanofi

4 parts

1. Grant requirements
2. Review process
3. Sharing of my own grant comments
4. Addressing comments

Am I good at grant writing? GRF

The project :

Scientific/scholarly merit	**Excellent**	**Very Good**	**Good**	**Fair**	**Poor**
	◉	○	○	○	○
Duration Proposed	**Too Long**	**Appropriate**	**Too Short**		
	○	◉	○		
Impact of Research	**High**	**Moderate**	**Low**	**None**	
	◉	○	○	○	

The principal investigator :

Ability to undertake the proposal	**Excellent**	**Very Good**	**Good**	**Fair**	**Poor**
	◉	○	○	○	○
Track record in field	**Excellent**	**Very Good**	**Good**	**Fair**	**Poor**
	◉	○	○	○	○

Scientific/scholarly merit	**Excellent**	**Very Good**	**Good**	**Fair**	**Poor**
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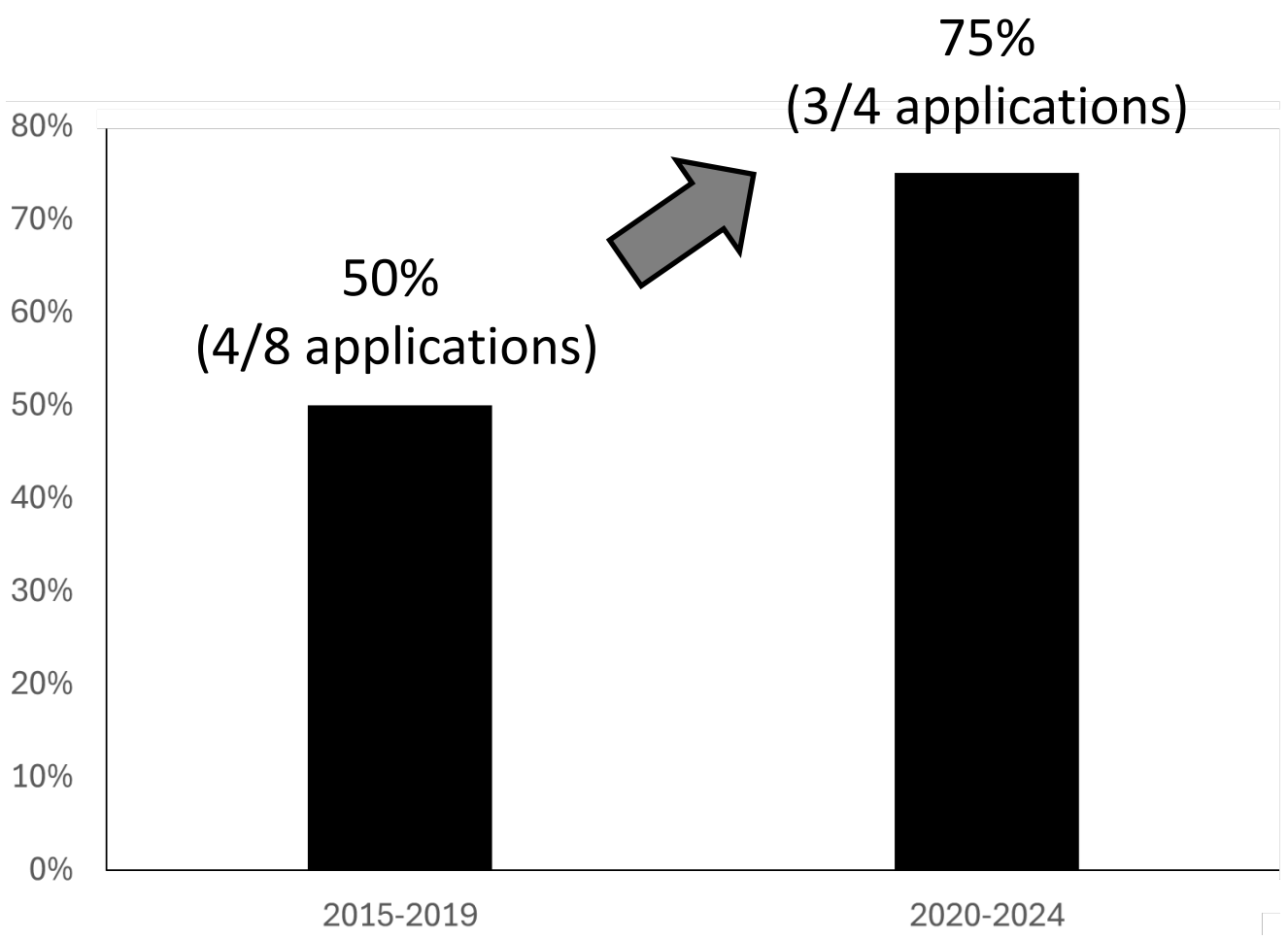
Funding Scheme :	General Research Fund (GRF)
Project Number :	
Exercise Year :	2023 / 24
Project Title :	
PI Name :	Prof Cheung, Ching Lung
Institution :	The University of Hong Kong
Project Fund :	N/A
Result :	3.5 (Detailed description)
Approved Project duration :	N/A
Notes for the Applicants :	RGC's policy on providing feedback to applicants

GRF: 20%
(2/10 applications)
5/5 x 1
4.5/5 x 1
3.5/5 x 8

Am I good at grant writing? HMRF

HMRF 2024: The success rate over the last three years is on average around 23%.

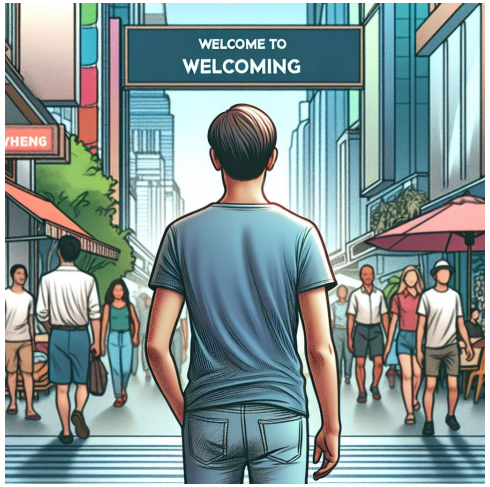


Success rate of my PDF:
42.9%
(3/7 applications)

Understanding the grant (HMRF)

- The HMRF aims to build research capacity and to encourage, facilitate and **support health and medical research** to inform **health policies**, improve **population health**, strengthen the **healthcare system**, enhance **healthcare practices**, advance **standard and quality of care**, and promote **clinical excellence**, through generation and application of evidence-based scientific knowledge derived from local research in health and medicine.

Understanding grant requirement



- For clinically relevant research projects, HMRF may be a good place for you

- If you are a basic scientist and want to illustrate a molecular role of a gene/ protein/ pathway, HMRF may not be a good place for you

HMRF: 4 broad areas

- Public health, human health and health services research
- Infectious diseases
- **Advanced medical research**
- Health promotion projects

Advanced medical research

Advanced medical research shall be **clinical studies** which apply advanced technologies to facilitate the translation of knowledge generated from health and health services or infectious diseases studies into clinical practice and to inform health policy.

Examples of clinical studies include clinical trials on effectiveness of disease treatment using genome editing technologies (such as CRISPR/Cas9) and their derivative reagents as gene editing tools; clinical applications of sequencing technology for disease diagnosis, prognosis and treatment strategies; development of machine learning and artificial intelligence approaches for drug treatments, surgical procedures, systemic therapy and radiotherapy with evaluation in clinical practices.

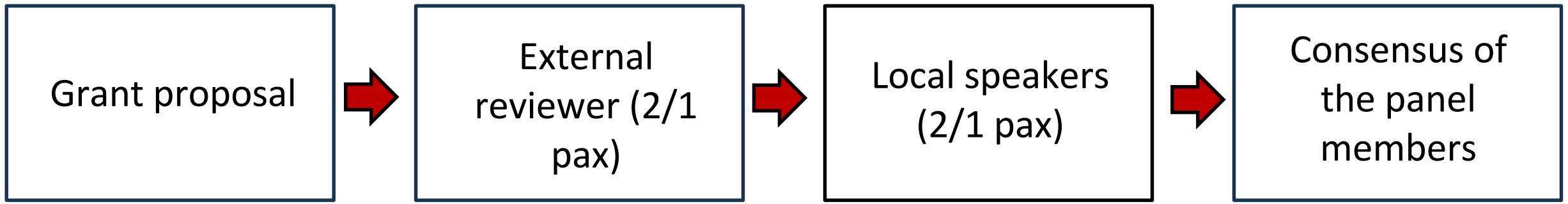
Other examples which apply advanced technologies to evaluate treatments and therapeutic interventions in clinical, community or applied settings include **clinical application and evaluation of** pharmaceuticals; cellular, tissue and gene therapies; medical devices; surgical, obstetric and dental interventions; radiotherapy and other non-invasive therapies; psychological and behavioural approaches, etc.

Review process

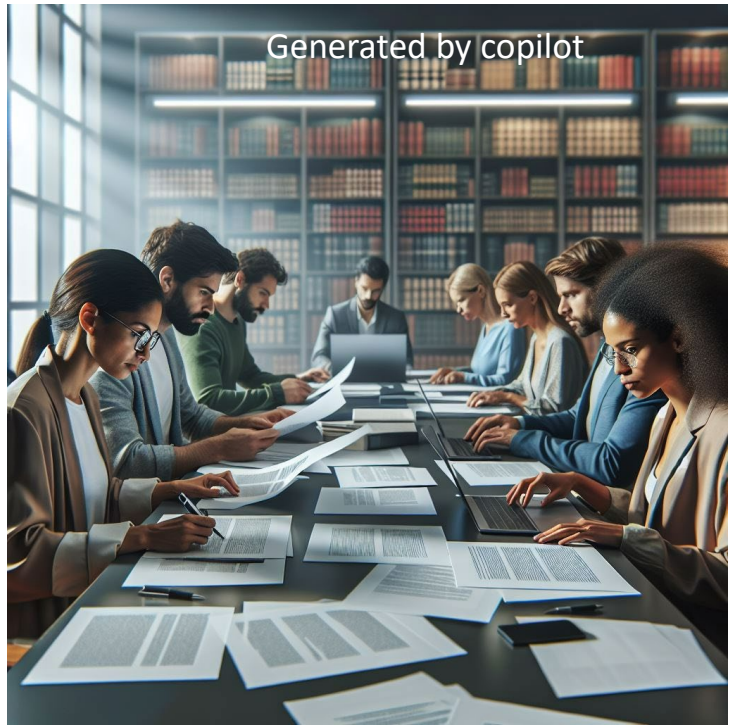
Referee's Assessment Form

1. Originality and Impact
2. Research Questions, Aims and Hypotheses:
3. Subjects and Study Methodology:
4. Outcomes and Data Analysis:
5. Research Capability:
6. Budget:
7. Ethical and Safety Considerations:
8. Overall Comments and Conclusion:
9. Confidential Comments to the Research Council (if any):

Two-tier review system



Reviewers



- Reviewers are humans
- They are busy
- Writing is important, try to give them an easy job instead of a hard job
- Writing a good and easy-to-understand proposal is important

Grant report sharing

HKU Med

A funded project

- 2023/2024 – Development and validation of sex-specific mortality prediction models among hip fracture patients: a machine learning study

- **What are the novelty, impact, and translational value (clinical practice/ policy) to Hong Kong?**

Originality and Impact

What is the importance of the proposed research in terms of its originality and potential impact in the area under study? How will the research findings benefit patients and/or the healthcare system? Will the research findings improve patient care, population health, influence clinical practice and/or health services management, or inform health policy in Hong Kong and elsewhere? Have the potential facilitators and barriers to this impact being achieved been identified?

The proposal is aimed at the development and validation of sex-specific mortality prediction models among hip fracture patients using machine learning approaches. Previous studies (by other groups) exist on such a topic but using limited patient cohort, time frame and small number of variables. Current group already ran a preliminary - and successful - study on that topic (see Fig.1 for some results, p.33).
This topic is important (in Hong Kong and elsewhere) since hip fractures among elderly patient might result in severe consequences: " 1-year mortality rate in hip fracture patients is high. In Hong Kong, approximately twenty percent of patients die within one year after sustaining a hip fracture". Currently clinicians are reluctant to prescribe anti-osteoporosis drugs to hip fracture patients - especially those with limited life expectancy - even though anti-osteoporosis agents were found effective. Hence prediction of mortality for those patients is indeed important (to better take care of them) and should reduce costs for the Hong Kong health care system, once implemented.

Research Questions, Aims and Hypotheses

How specific, clearly expressed and realistic are the research questions, aims and hypotheses?

The aim is clear (see paragraph above) and hypothesis also, that is: the "use of big data (> 100 variables) from a population-based EHR with a large sample size (> 60,000 hip fracture patient database is available) will provide sufficient power and information to enable the
development of an accurate prediction tool for mortality".
Based on the applicant preliminary study, this is much appropriate indeed (they used only 46 parameters and a limited number of patients in their initial study).

Preliminary data → whether your project is realistics

Subjects and Study Methodology

(i) Is the proposed design and methodology appropriate for the study? (ii) Are sample sizes clear, justified, adequate and realistic? (iii) Are any preliminary data available? (iv) How feasible is the proposed timeframe? (v) Please also provide comments on the following (where applicable):

(i) It is appropriate, although the applicants did not discuss much about: "Thus, we plan to conduct a clinical trial to evaluate the tool's effectiveness in reducing a second fracture and other clinical outcomes. (p. 9)" This is a key point since by using the 5-year data as applicants plan to do, the dead rate should be established with an high confidence level. However what is to be expected with only preliminary data from a patient recently tested (and obviously still alive)?
All the usefulness of the project is related to that aspect: How accurate will be the prediction in the presence of preliminary data? This aspect should be discussed in details. A secondary question is: How the dead rate will be affected if care is given to the patent (ex: following administration of anti-osteoporosis drugs)?
The other point is related to the '100 variables', it is discussed p. 4 in one paragraph "Predictor variables' but more details could have been added: what?, why?, how data will be extracted from medical records, etc.

Subjects and Study Methodology

(i) Is the proposed design and methodology appropriate for the study? (ii) Are sample sizes clear, justified, adequate and realistic? (iii) Are any preliminary data available? (iv) How feasible is the proposed timeframe? (v) Please also provide comments on the following (where applicable):

(ii) Applicants plan to use an available database of 69,599 patients, they already ran tests with 58,171 patients with good results (Fig.1, p.33). This appears well appropriate. Interestingly, applicants exclude the Covid Pandemic patients due to the unrelated mortality cases.

(iii) Yes, on 58 171 patients.

(iv) 21 months as indicated appear appropriate (p. 9), especially since the data is already available. What is unclear is the time table (p. 29). For instance the Research Assistant is hired for 18 months (p.13) . We understand some task will overlap but we do not know which one. Details would be needed.

(v) Yes, it falls under: " E-0002 : Apply big data analytics to examine clinical information for prevention, diagnosis, therapeutics, rehabilitation and better management of patients". This is relevant and appropriate.

Outcomes and Data Analysis

(i) Are the primary and secondary outcomes clearly defined? (ii) Have potential problems been anticipated and addressed? (iii) Is the statistical/analytical design appropriate and clearly explained?

They want to : "to conduct a clinical trial to evaluate the tool's effectiveness in reducing a second fracture and other clinical outcomes." This is very important to assess the value of the work (p. 9). They want also: "prepare an online tool that is open for public and healthcare professionals use." (p. 6).
The outcome include also publication, conference , p. 5 (without details: where,?, how many?).
All of this is very appropriate.

Research Capability

Comment on (i) the research team's expertise and track record (incl. principal investigator / project team members / collaborators) and (ii) the existing facilities of the Institution where the research will be conducted.

(i) The team comprises the Principal applicant (PA) an a colleague. The PA specializes in osteoporosis, with extensive experience in big data study using advanced statistical models. The PA has published extensively and is active in several other projects (p. 18, para 11.b), this is a good sign of the potential success of the current proposal since some of these projects are completed (and 'related' by some aspects although there seems to be no overlap with the current proposal).

The Co-Applicant (CA) is a clinical professor and will provide advise on the study especially in the clinical insight.
There will also be a Research Assistant for 18 months (out of the total project duration of 21 months).
I consider the team appropriate and sufficient considering the tasks to be done (p. 29).

(ii) Applicants have access to high performance computing service providing computational power to the proposed project (p. 5), this appears well appropriate.

Budget

Is the request for research personnel, consumables, equipment and overall budget justified and reasonable?
[For reference, 1 USD is equivalent to approximately 7.8 HKD]

Budget is mainly for one Research assistant, publication, conference, computing and audit fees. It looks quite appropriate and is well-justified.

Ethical and Safety Considerations

Is the proposed research ethically sound? Outline any safety or ethical issues that from the proposed research and comment on whether these have been adequately addressed in the proposal. Has ethical approval been sought?

Ethical approval will be requested if project is granted (p. 30).

Overall Comments and Conclusion

It is always helpful for applicants to receive constructive feedback from reviewers. What are the specific strengths and weaknesses of this proposal? Please include a brief overall appraisal of the proposal focusing on any areas for improvement and the basis for your comments, e.g. awareness of other work in the field.

Strengths:

- Sound aims and hypothesis.
- Proven preliminary trials.
- Large available data.
- Good team (PA, CA, RA) with good research track record relevant to the proposal (for PA, CA) .
- Realistic time frame and budget.

Weaknesses:

- See above my comments on partial available data for incoming patients, effect of treatment.
- See above my comments on the '100 variables'

- All acronyms need to be defined once they appear, now some miss their appropriate definition (PA - Principal Applicant, ROC - Receiver Operating Characteristic curve, etc.)

Addressing comments

Grant Review Board's comments

GRB's comments

1. Justify the rationale for examining sex-specific factors solely in the associations with hip fracture and mortality.

2. Elaborate on the definition and selection criteria of the ">100 variables" that will be used as predictors (see Reviewer 1's comments for details).

3. Clarify whether there are sufficient data for prediction of a second fracture.

4. Elaborate on the proposed database in comparison with other international database.

5. Elaborate on the clinical implications of the findings.

6. Provide further clarification and breakdown for the following budget item: "High computing services" ($10,000) with a written quotation.

7. Provide evidence such as a letter of support from the relevant authority (e.g. Hospital Authority) that the data provider will provide the necessary data to the project team in the appropriate format. Clarify if a fee is required and revise the budget accordingly.

8. Human research ethics approval from a recognised ethics committee is required.

How to address reviewers' comments?

- I am sorry to say that "**reviewers are always right**" (this is the rule of the game)

- **Interpersonal and communication skill is important**

When your reviewers' comments are wrong…

https://news.ifeng.com/history/shijieshi/200908/0820_7182_1311811.shtml

- It can be challenging to address a situation where you believe your reviewers' comments are incorrect. Here are some strategies to do so **politely** and effectively:
  - **Choose the Right Time and Place**: Find a suitable moment to discuss the issue privately with HMRF Secretariat. Avoid bringing it up in front of others to prevent any embarrassment.
  - **Acknowledge Their Perspective**: Start by acknowledging HMRF Secretariat's/reviewer's viewpoint. This shows respect and understanding. For example, you could say, "I understand your point about..."
  - **Use Cautionary Language**: Instead of directly saying they are wrong, use phrases like "I think there might be a different perspective on this" or "I believe there may be another way to look at this."
  - **Provide Evidence**: Back up your point with facts or data. This makes your argument more credible and less about personal opinion. For example, "Based on the data we have, it seems that..."
  - **Focus on the Impact**: Explain how the mistake might affect the project or the team. This shifts the focus from who is right or wrong to what is best for the project / study. For instance, "I'm concerned that this approach might lead to..."
  - **Suggest Solutions**: Offer constructive alternatives or solutions. This shows that you are not just criticizing but also thinking about how to improve the situation. For example, "Perhaps we could consider..." **(Answer generated from co-pilot)**

Pray for good luck

- The system is not perfect
- Reviewers/ GRB members are not perfect
- Keep calm and carry on

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