

Effects of Exercise on Persons with Metastatic Cancer

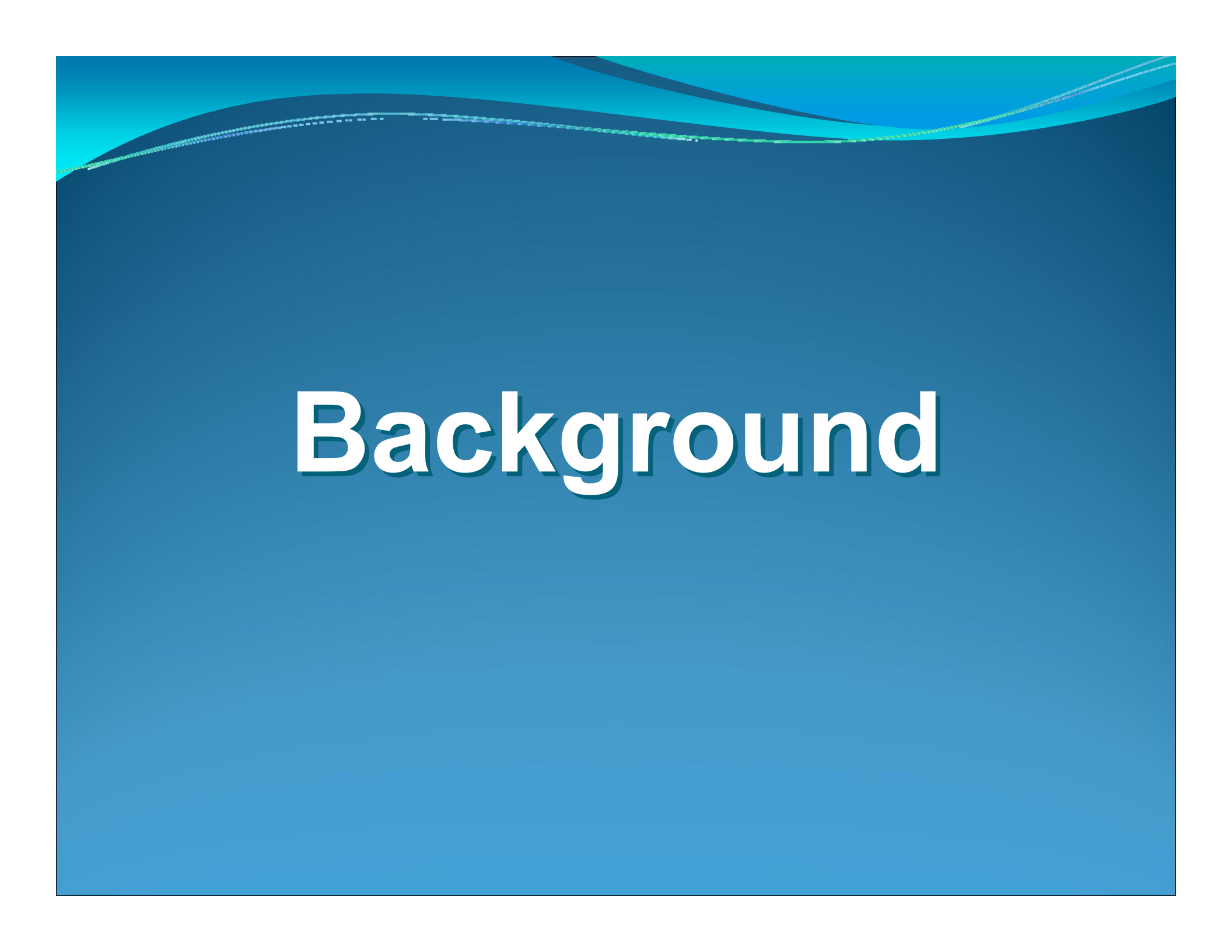


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Outline

- Background
- Methods
- Results
- Discussion
- Conclusion
- Acknowledgements



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Background

Cancer Statistics

- The Canadian Cancer Institute estimates that in 2008, in Canada there will be:
 - 166,400 new cases of cancer
 - 73,800 cancer-related deaths¹
- Of persons with a new cancer diagnosis 30% will already have metastatic disease²
- Once metastasis has occurred, prognosis is generally poor³

Metastatic Cancer

- Creates different challenges than that of non-metastatic cancer as it is a palliative disease⁴⁻⁸
- It causes declines in quality of life (QOL), psychological barriers and fatigue⁴⁻⁸
- Persons with metastatic cancer are now living longer⁹
- Suggest the need for research on interventions aimed at improving QOL

Previous Research

- Focused on exercise interventions for persons with local or regional cancer¹⁰⁻¹⁴
- Many reviews investigated the impacts of exercise on fatigue^{7,10-15}
- Fatigue is a prevalent symptom
 - 90% of persons with cancer experience cancer-related fatigue⁶
- Cancer-related fatigue has also been linked with symptoms of anxiety and depression⁶

Previous Research

- Demonstrated physical exercise is an effective intervention to improve QOL & fatigue in persons with non-metastatic cancer^{7,10-15}
- Traditionally, persons with metastatic cancer were encouraged to rest⁷
- Rest is no longer considered an appropriate intervention
- New literature is emerging regarding the potential benefits of exercise for persons with metastatic cancer^{5,7,16,17}

Purpose

To synthesize the available literature on the effects of exercise on QOL and physical measures in persons with metastatic cancer





Review Questions

1. What exercise interventions are being used for persons with metastatic cancer?
2. What is the effect of these interventions in respect to QOL and physical measures?
3. What research needs to be completed in the future?
4. Investigate the adverse effects and attrition rates documented in the studies.



Definition of Metastatic Cancer

- The spread of cancer from one part of the body to another³
- For the purpose of this review it includes:
 - advanced cancer
 - palliative cancer
 - stage IV cancer
- Frequent sites of metastases include:
 - lung, liver, breast & bone⁹

Quality of Life (QOL)



Exercise

- “Any planned, structured, and repetitive bodily movement done to improve or maintain one or more components of physical fitness”¹⁹



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Methods

Search Strategy

Up to and including May 8, 2008



Databases:

- Medline, Embase, CINAHL, PsychInfo, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Databases of Systematic Reviews (EBM Reviews-Ovid) and PEDro

Keywords:

- metastatic OR palliative OR advanced
AND
- cancer OR neoplasm
AND
- exercise OR physical activity OR exercise therapy OR physical fitness

Inclusion Criteria



- **Population:** persons with metastatic or advanced or palliative cancer
- **Intervention:** exercise as the intervention or a component of the intervention
- **Publication:** in a peer-reviewed journal
- **Comparisons and outcome measures:** not screened at the initial stages to include all relevant studies

Exclusion Criteria



Population:

- Persons with lymphoma, melanoma or myeloma
- Less than 50% of the sample had metastatic or advanced cancer
- When results of those with metastatic cancer could not be separated from those with non-metastatic cancer

Type:

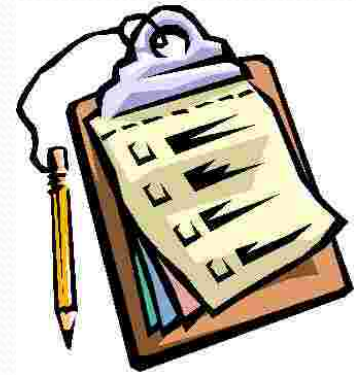
- Studies in a language other than English or French
- Newspaper editorials, single article reviews and qualitative research studies

Data Extraction



- Tool developed by reviewers
- Pilot tested by two reviewers
- Extraction was performed on each study by one reviewer and then checked by a second reviewer
- Data extracted from 12 studies: methods, participants, inclusion/exclusion criteria, intervention, attrition, adherence, and outcomes.

Quality Assessment



Randomized Controlled Trials (RCT's)

- Modified van Tulder Criteria²⁰
 - One criterion added: "Was the study's purpose clearly stated?"
 - Low = 0-4, Medium = 5-8, High = 9-12

Case Series

- Modified Case Series Criteria²¹
 - Removal of criterion 6: comparison of sub-series
 - Low = 1-2, Medium = 2.5-3.5, High = 4-5

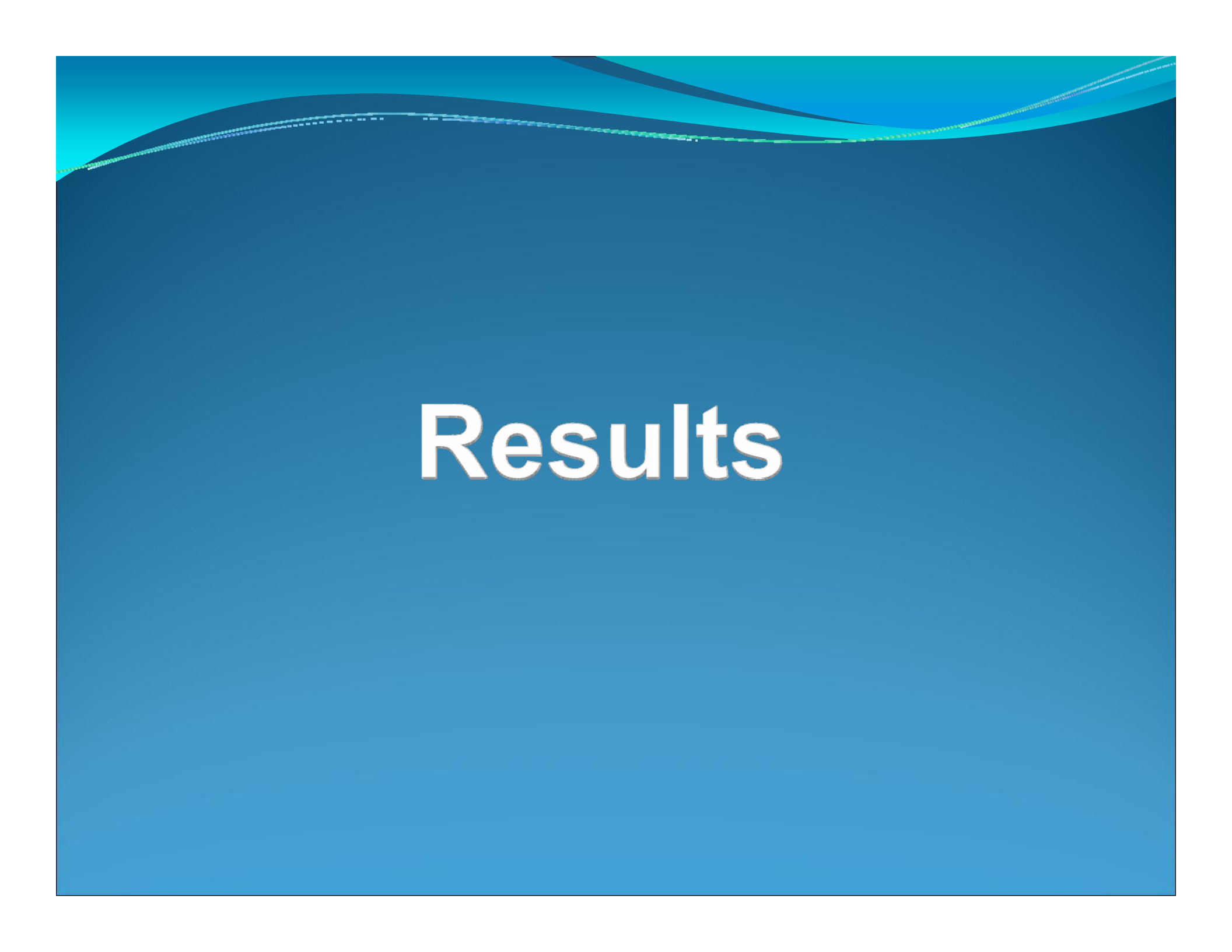
Case Reports

- Case Study Methodological Quality Assessment Tool²²
 - Low = 1-3, Medium = 4-5, High = 6-7

Data Synthesis

- Study characteristics were compiled in a table
- Meta-analysis was not possible due to study heterogeneity in:
 - Study populations
 - Exercise interventions
 - Outcome measures
 - Study designs



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Results

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graph TD; A[Titles reviewed after initial search of databases  
Total = 674] --> B[Studies included after title screening  
N = 224  
(100% Agreement)]; B --> C[Articles found through hand searching  
N = 1]; B --> D[Abstracts reviewed  
N = 225]; C --> D; D --> E[Full text reviewed  
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(96% Agreement)];
```

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12 Included Studies: 5 RCT's

- **Rummans**²⁴: 103 persons with advanced cancer of various primary sites participated in a multi-dimensional exercise program for 3 weeks
- **Brown**⁴: 115 persons from the Rummans et al.²⁴ study, followed for 4 weeks to investigate if improvements in quality of life (QOL) impact fatigue in patients
- **Lapid**²³: Geriatric subgroup of 33 persons from the Rummans et al.²⁴ study followed for 4 weeks
- **Headley**¹⁶: 38 women with advanced breast cancer completed seated exercises for 12 weeks
- **Segal**²⁵: 60 men with palliative prostate cancer completed resistance exercises for 12 weeks

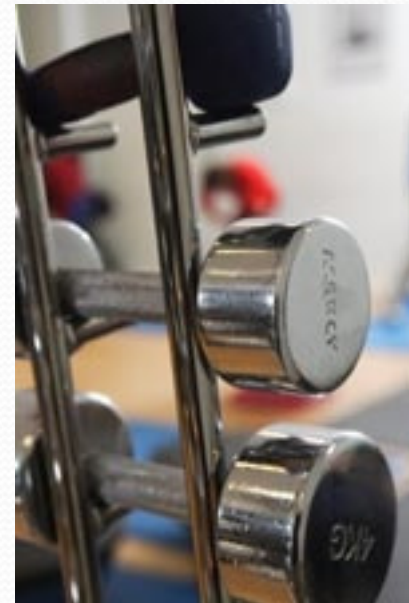
12 Included Studies:

5 Case Series

- **Oldervoll**²⁶: 52 persons w/ metastatic cancer of various 1° sites completed circuit training, standing balance & aerobic endurance ex's for 6 wks
- **Adamsen, 2003**²⁷: 27 persons w/ advanced cancer of various 1° sites participated in a multi-dimensional intervention: resistance ex & stationary cycling for 6 wks
- **Adamsen, 2006**²⁸: As per Adamsen 2003²⁷ w/ 115 participants
- **Carson**²⁹: 21 women with metastatic breast cancer performed yoga exercises for 8 wks
- **Porock**⁷: 9 persons w/ metastatic cancer of various 1° sites performed individual home exercises for 2-4 wks

12 Included Studies: 2 Case Reports

- **Crevenna**³⁰: 1 female with metastatic breast cancer performed ergometric cycling for 1 year
- **Kelm**³¹: 1 male with metastatic adenocarcinoma of the rectum completed endurance training and strength exercises for 13 weeks



And then there were TEN

- Rummans et al.²⁴, Brown et al.⁴ & Lapid et al.²³ were based on the same study sample
- To demonstrate the breadth of literature all 3 studies were included in the characteristics table
- To prevent skewing of the results, only Rummans et al.²⁴ was included in the text of the results & discussion sections, resulting a total of **10 studies**

Study Characteristics

Population

- *Cancer status:* five studies^{25,26,29-31} metastatic, four studies^{16,24,27,28} advanced and one study²⁵ palliative
- *Primary cancer sites:* varied
- *Concurrent treatment:* eight studies included persons undergoing concurrent chemotherapy & four studies included persons undergoing radiation therapy



Characteristics of the Studies

Intervention

- *Type*: included yoga, balance, coordination, aerobic & strength training
- *Frequency*: generally 2-3 x/wk for 3-13 wk
- *Intensity*: strength @ 40-95% of 1RM^{25,27,28,31} & aerobic @ low-moderate intensity^{7,30,31}

Most Frequent Outcome Tools

- *Physical measures*: 1RM^{27,28,31} & VO2 max^{27,28,30}
- *QOL measures*: EORTC QLQ-30²⁶⁻²⁸ & the SF 36^{27,28,30}

Inclusion & Exclusion Criteria

Differed across studies in regards to:

- Life expectancy e.g. Porock⁸ versus Oldervoll²⁶
- Co-morbidities e.g. bone metastases/lesions
- Mental health status e.g. Adamsen²⁸

Attrition, Adherence & Adverse Effects



Attrition:

- RCT's –ranged from 7-16%
- Case Series –ranged from 14-35%
- Case Reports –0%

Adherence: ranged from 75-100%

Adverse Effects: no adverse effects were noted

Quality Assessment - RCT's

- Three RCT's assessed with the modified van Tulder Criteria²⁰
- All were rated as high quality (9/12)
- All failed to conceal the treatment allocation and blind the patient to the intervention (criterion C & D)
- Two studies^{24,25} did not blind the therapist to the intervention (criterion F)
- Headley et al.¹⁶ was able to blind the therapist to the intervention (criterion F)

Quality Assessment - Case Series

- Five case series were assessed with the modified Case Series Criteria²¹
- All five studies were rated as medium quality
- None of the case series were able to fulfill blinding (criterion 5.2) or representative sampling (criterion 1)
- Carson et al.²⁹ did not have explicit inclusion criteria (criterion 2)

Quality Assessment - Case Reports

- Two case reports were assessed using the Case Study Methodological Quality Assessment Tool²²
- Crevenna et al.³⁰ was rated high quality (6/7)
- Kelm et al.³¹ was rated medium quality (4/7)
- Both failed to clearly state their hypothesis (criterion B)
- The effect size in the Kelm et al.³¹ study was not clinically important (criterion F) and limitations were not identified (criterion G)

Levels of Evidence

Assigned using the Oxford Centre for Evidence-Based Medicine (CEBM) Levels of Evidence³²

Three RCT's = 2B

Five case series = 4

Two case reports = 5





Oxford CEBM Level 2B

Improvements in physical measures including:

- Increased upper and lower extremity muscle endurance²⁵

Improvements in QOL measures including:

- Improved quality of life^{16,24,25}
- Increased overall spiritual well being in the intervention group, and increased emotional distress in the control group²⁴
- The intervention group experienced a slower decline in total QOL¹⁶

Oxford CEBM Level 4

Improvements in physical measures including:

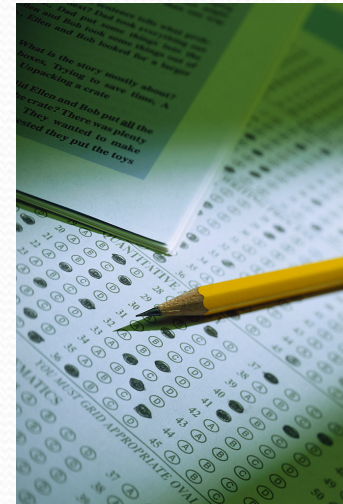
- Increased strength and aerobic fitness^{27,28}
- Increased physical activity²⁸
- Increased walking distance and faster sit-to-stand²⁶



Oxford CEBM Level 4

Improvements in QOL measures including:

- Increased levels of invigoration and acceptance³⁰
- Decreased physical fatigue²⁶
- Increased role emotional, social and dyspnea subscales²⁶
- Improved role-physical score²⁸
- General increase in QOL²⁹
- Decreased anxiety⁸

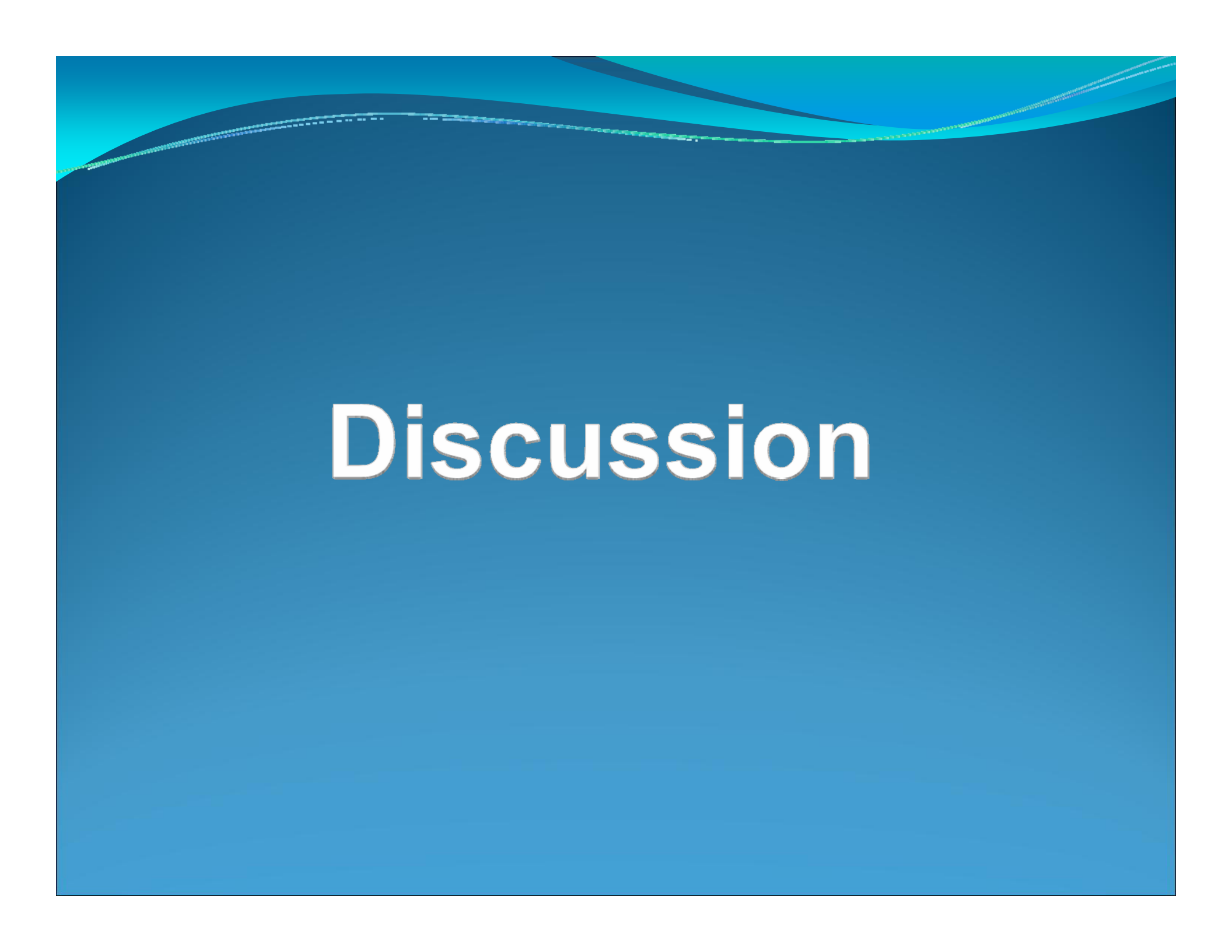


Oxford CEBM Level 5

Improvements in physical measures including:

- Increased aerobic fitness^{30,31}
- Improved respiratory function³¹
- Increased or maintained 1 RM³¹



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Discussion

Limitations

Heterogeneity of:

- study samples
 - decreased external validity
- exercise interventions
 - unable to determine optimal frequency, intensity, exercise type and session duration
- outcome measures
 - No single measure for QOL³³

Limitations

Outcome Measures

- Reliable and valid outcome measures found to be most widely used^{25,34-37}:
 - European Organization for Research and Treatment of Cancer QOL Questionnaire Core 30 (EORTC-QLQ-C30)
 - Functional Assessment of Chronic Illness Therapy (FACIT)
 - Symptom Distress Scale (SDS)
 - 36-Item Short Form (SF-36)
 - Multidimensional Fatigue Inventory (MFI)
 - Hospital Anxiety and Depression Scales (HADS)

Attrition

- Short life expectancy and debilitating symptoms make retention of participants challenging
- It could be expected that attrition rates would be higher than normal for this population³³
- However, all 10 studies have attrition rates well below normal range



Adherence & Adverse Effects

- Documented adherence rates ranged from 75% to 100%
- No comment on potential reasons
- Speculation: individualized programming, group participation or even noticeable improvements as motivators?
- No adverse effects documented



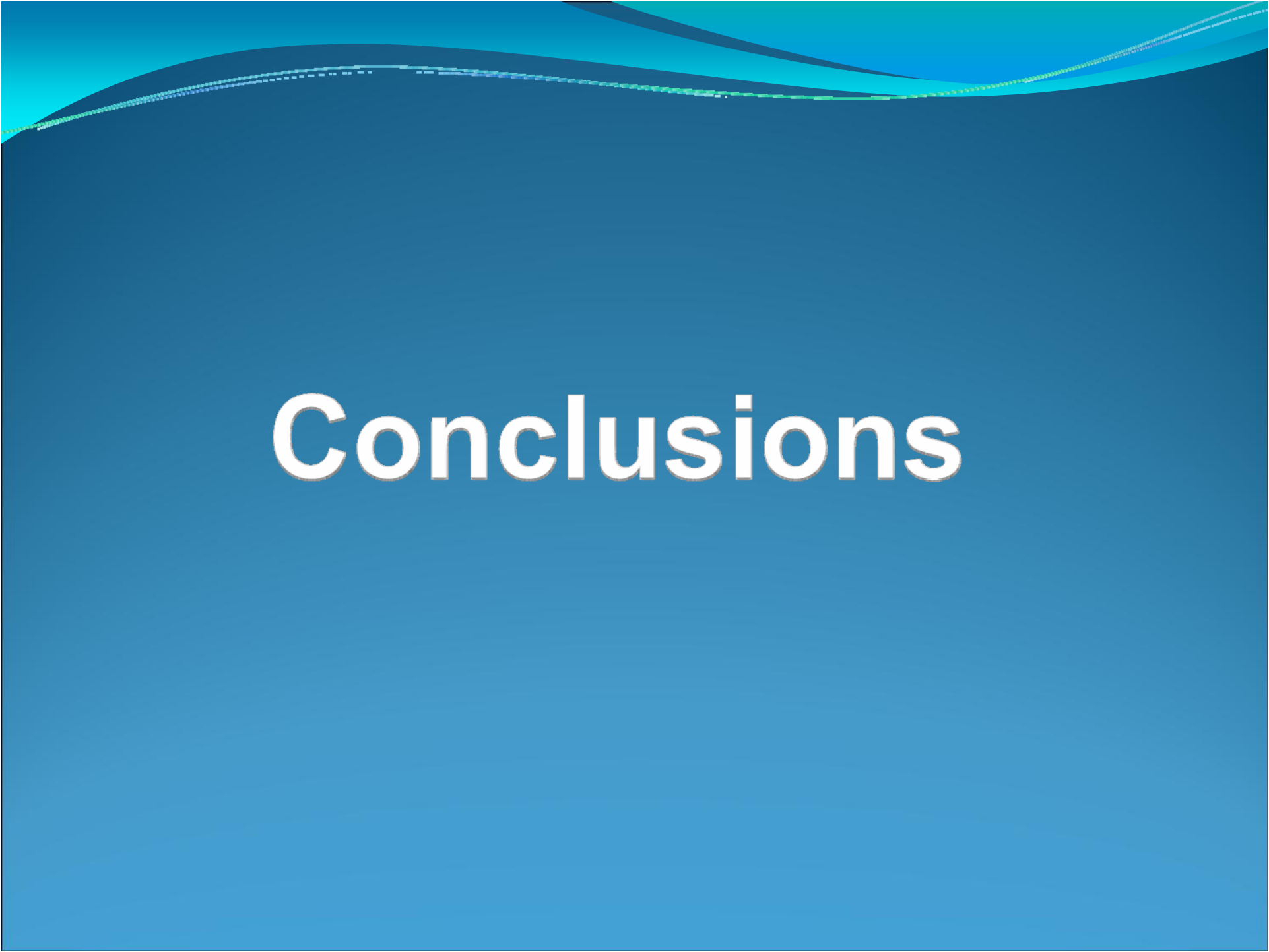
Implications for Future Practice

- Provides evidence to support exercise as a safe and effective intervention for persons with metastatic cancer
- Unable to direct a specific exercise prescription
- Exercise has a positive effect on QOL and physical status
- Important to communicate benefits and goals of exercise to patients and their families



Recommendations for Future Research

- Conduct larger and more rigorous RCT's
- Investigate metastatic cancer sub-groups
- Use consistent terminology to define cancer status
- Determine acceptable attrition rates
- Clarify optimal (or minimal) exercise prescription
- Use consistent outcome measures

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Conclusions

Concluding Statements

1. There is a positive association between exercise and changes in both QOL and physical status.
2. Clinicians working with persons with metastatic cancer should use caution with exercise prescription, as there is currently no agreement upon optimal exercise parameters.
3. Further research in the area should focus on large-scale RCT's to identify optimal and safe exercise parameters for this population.

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Questions and Discussion



