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Impacts on health outcomes and on resources utilization for home based parenteral chemotherapy administration: a systematic review protocol

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ABSTRACT

INTRODUCTION:

Despite policies, in a few countries, to enable more to receive chemotherapy at home and despite the demonstrated feasibility, the parenteral chemotherapy administration at home remains currently marginal. Of note, findings of different studies on health outcomes and resources utilization vary leading to conflicting results. This protocol outlines a systematic review that seeks to synthesize and critically appraise the current state of evidence about the comparison between home setting and hospital setting for the parenteral chemotherapy administration within the same high standards of clinical care.

METHODS AND ANALYSIS:

This protocol has been prepared following the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (P-PRISMA) approach. Electronic searches will be conducted on bibliographic databases selected from the earliest available data through November 15th, 2017 published in French and English languages. Additional potential papers in the selected studies and grey literature will be also included in the review. The review will include all types of studies exploring patients receiving anti-cancer drug for injection at home compared to patients receiving the drugs in hospital setting and will assess at least one of the following criteria: the patients' health outcomes, the patients 'or caregivers 'satisfaction, the resources utilization with cost savings, the incentives and/or the barriers of each admission setting according to the patients and relatives' point of view. Two reviewers will independently screen studies and extract relevant data from included studies. Methodological quality of studies will be assessed using the "Quality Assessment Tool for Quantitative Studies" developed by the Effective Public Health Practice Project (EPHHP) tool in addition to the Drummond checklist for economic studies.

ETHICS AND DISSEMINATION: As the review is focused on the analysis of secondary data, it does not require ethics approval. The results of the study will be disseminated through articles in peer-reviewed journals and trade publications as well as presentations at relevant conferences.

PROTOCOL REGISTRATION: International Prospective Register for Systematic Reviews (PROSPERO) number CRD42017068164.

KEYWORDS: systematic review - chemotherapy -Hospitalization At Home- cancer care -Costs -Home Care - Quality Of Life

STRENGHTS AND LIMITATIONS OF THIS STUDY:

- This will be one of the first attempts to synthesize and critically appraise the current state of evidence about the comparison between home setting and hospital setting for the parenteral chemotherapy administration in the same high standards of clinical care. The systematic review protocol is developed using the Preferred Reporting Items for Systematic Reviews and meta-analyses for Protocols (PRISMA-P) guidelines and includes the search to literature published in two languages and the wide search from published studies to the grey literature.

- Methodological quality of studies will be assessed using the "Quality Assessment Tool for Quantitative Studies" developed by the Effective Public Health Practice Project (EPHHP) tool in addition to the Drummond checklist for economic studies.

- Based on previous work, we anticipate methodological heterogeneity and statistical heterogeneity leading to difficulty to analyze data quantitatively.

- The definition of home-based services is confusing including different types of interventions leading to discrepancies when analyzing.

INTRODUCTION

Hospital remains the main setting for parenteral cancer chemotherapy administration despite the patient's general positive feeling about receiving care at home,[1]. As the worldwide incidence of cancers increases,[2] and, bearing in mind that due to progress in efficacy of treatments, cancer is becoming a long-term disease, along with advances in diagnostic technology and novel targeted treatments, with their financial constraints, it is necessary to develop alternative models of health service delivery such as home programs, without detrimental effects on health outcomes and costs. Despite the feasibility,[3-5] and despite policies to enable more to receive chemotherapy at home, in a few countries,[6,7], the parenteral chemotherapy administration at home remains marginal due to little evidence, for improving the health outcomes, for patient's quality of life and for cost savings. Furthermore, findings on outcomes varied leading sometimes to conflicting results,[8-10]. A recent scoping study demonstrates most economic studies concluded in favor of home care, but according to the appropriate type, all sources of expenditure (specialized clinical care, transportation, out-of-pocket expenses, etc…) were not systematically assessed,[11,12] whereas other studies showed no significant difference in the overall costs,[9,10]. Likewise, the impacts on caregivers especially the shift of the care burden from hospital to relatives have rarely been studied. To date, only one existing review of home-based chemotherapy,[13] and it ended in favor of administration at home but, this conclusion is hampered by a mix between routes of administration (parenteral and oral intake) and type of care (administration and post administration follow-up).

Considering these facts, a systematic review will be undertaken for providing a complete overview of parenteral cancer chemotherapy administration at home to investigate whether the clinical outcomes are maintained and the resources utilization are reduced in comparison to hospital high standard care.

METHODS:

This protocol has been prepared following the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (P-PRISMA) approach,[14] to increase the confidence in the findings. It has been registered in International Prospective Register of Systematic Reviews database (no CRD42017068164).

Types of studies

All types of studies that have investigated the parenteral cancer chemotherapy home administration compared to hospital setting as randomized, controlled or uncontrolled trials, cohort studies, parallel, or cross-over studies will be included if they fulfill at least one of the following criteria:

1) Assessment of the impact of parenteral chemotherapy administration on patients' health outcomes, whatever they are: survival, relapse, tolerance

2) Assessment of the impact of parenteral chemotherapy administration on patients 'or caregivers 'satisfaction

3) Assessment of the impact of parenteral chemotherapy administration on cost savings

4) Assessment of the incentives and/or the barriers according to the patients and/or relatives' point of view

Participants:

We will be interested in studies on participants receiving parenteral anti-cancer drug administration at home compared to patients receiving the drugs in a hospital setting. There will be no restriction concerning the type of tumor disease, age or sex of participants.

Eligibility criteria

All studies exploring parenteral anti-cancer drug administration at home setting, mainly intravenous and subcutaneous administration, will be selected from the earliest available data through November 15th, 2017 published in French and English languages, whatever the country. The inclusion criteria defining the scope of publications included in the review will be the comparison of parenteral chemotherapy administration at home with administration in-patients and/or out-patients wards.

As our goal is to study the home-based setting as an alternative context for providing the highest standards of clinical care concerning the parenteral drug delivery, we will exclude all community-based services with no anti-cancer drugs administration at home and the studies targeting only the post-administration chemotherapy monitoring, the disconnection of portable diffusor, the management of central venous catheter, and the supportive care therapy. For the same reasons, studies about oral anticancer drugs will be excluded as the oral treatment does not require hospital care, patients usually manage their pills themselves with an ambulatory follow-up and the treatment issues are deeply different (i.e chronic side effects, patient's compliance).

Databases and Search strategy:

A detailed literature search will be conducted to identify all articles studying chemotherapy administration in home setting for adults and pediatrics patients. Published studies will be identified through searches of the Medline, Cochrane, Web of Science databases, Embase and Cumulative Index of Nursing and Allied Health (Cinahl) from the earliest available date through November 15th, 2017. We have developed a strategy in Medline to retrieve relevant literature on the topic. The MEDLINE search strategy will be

("Neoplasms"[Mesh] AND ("Antineoplastic Combined Chemotherapy Protocols"[Mesh] OR "Antineoplastic Agents"[Mesh])) AND ("Home Care Services"[Mesh] OR "Home Care Agencies"[Mesh]). This search strategy will be adapted in searching other databases. The references from potentially relevant papers were manually searched for additional studies. A further research will be performed in Opengrey, in Research papers in Economics (RePec) and in Google Scholar databases to find relevant unpublished studies in grey literature.

Study selection:

We will use a two-stage process for the identification of papers that met our inclusion criteria. The first stage accumulated all papers from the two types of searches using the already mentioned databases. The first type of search will use combinations of keywords to retrieve titles of potentially relevant studies. The search output will be screened independently by two review authors (MDS, BMM) to identify studies that potentially meet the inclusion criteria outlined above. In case of discrepancy, the abstract of the concerned study will be retrieved. If disagreements are remained, a third author (EB) will arbitrate. In the second type of search, all papers citing or cited by articles that had already met our inclusion criteria will be identified then screened as the first ones. In the second stage, the full text of these selected studies will be retrieved and independently assessed for eligibility by the same two review members. An article will be considered relevant and kept for analysis if the full text for the publication will be a comparison design assessing patient's health or/and safety outcomes or/and patients' or relatives satisfaction, or/and cost-savings or/and the incentives and the barriers of using home as an alternative setting. The duplicates of articles will be discarded.

Any disagreement between them over the eligibility of particular studies will be resolved through discussion with a 3rd reviewer (EB).

Data extraction

Extracted information to a standardized form will include:

- study setting

- study population

- tumor type and chemotherapy regimen

- details of the intervention/control conditions

- experimental design

- recruitment and study completion rates

- patients' health outcomes including Quality of Life, duration of survival, progression of disease, toxicity

- patients' and caregivers' satisfaction and preference, shift of burden,

- resources utilization with costs and consequences including cost-effectiveness, cost-utility or cost-benefit analyses, perspective of the study including provider, payer or societal and shift of costs

- Incentives and barriers according to the patients' and/or relatives' point of view

- Information for the assessment of the risk of bias

Data will be extracted independently by the two review members; discrepancies will be identified and resolved through discussion with a 3rd reviewer (PA).

Data assessment and synthesis:

Quality assessment

Two reviewers (MDS and BMM) will independently assess the quality of included studies and the potential risk of bias. We will use the "Quality Assessment Tool for Quantitative Studies" developed by the Effective Public Health Practice Project (EPHHP) tool,[15] as it can be applied to articles of any public health topic area , assessing the components of studies (design, methods, bias). Likewise, we will use the Drummond check-list [(16)], focusing on the design quality of the costs studies. It is leading to an overall methodological rating of strong, moderate or weak. Consensus will be reached through discussion in case of disagreement.

Data synthesis

According to the limited development of home parenteral chemotherapy administration, we anticipate methodological heterogeneity and statistical heterogeneity against a meta-analyze of the evidence base. Consequently, a narrative synthesis could be used to synthesize the data.

Subgroup analysis

If the data are available, we will conduct subgroup analyses investigating the effects of the study design, the effect of the tumor type (hematologic tumor, solid tumor) and the effects of the age of the study population (children, young people < 18 years old, adults, > 65 years old).

A sensitivity analysis will determine the robustness of the observed outcomes facing publication language, clinical or methodological heterogeneity.

Ethics and dissemination: As the review is focused on the analysis of secondary data, it does not require ethics approval. The results of the study will be disseminated through articles in peer-reviewed journals and trade publications as well as presentations at relevant conferences.

CONCLUSION

This review will be an attempt to synthesize and to critically appraise the impact on parenteral chemotherapy administration at home for the patients and their relatives compared to the hospital setting and, following the P-PRISMA guidelines.

Others strengths of this review include the search to literature published in two languages, French and English and the wide search from published studies to the grey literature.

It is although, acknowledged that the definition of home-based services is confusing including different types of interventions and could lead to discrepancies when analyzing. Likewise, the results of the review may be limited by the diversity of the study designs and present challenges in the quality assessment. These limitations will be considered in relation to the review findings.

However, this review could be useful for the medical staffs to choice the best treatment setting for patients and their relatives, contributes to develop the parenteral chemotherapy administration at home and highlights to define the realistic methodology to set up in this field.

Contributors: All authors made substantive intellectual contributions to the development of this protocol. BMM wrote this protocol. MDS, EB, PA commented critically the manuscript and involved in conceptualizing the review. JA commented critically the manuscript.

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ABSTRACT

INTRODUCTION:

Despite policies, in a few countries, to enable more to receive chemotherapy at home and despite the demonstrated feasibility, the parenteral chemotherapy administration at home remains currently marginal. Of note, findings of different studies on health outcomes and resources utilization vary leading to conflicting results. This protocol outlines a systematic review that seeks to synthesize and critically appraise the current state of evidence about the comparison between home setting and hospital setting for the parenteral chemotherapy administration within the same high standards of clinical care.

METHODS AND ANALYSIS:

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ETHICS AND DISSEMINATION: As the review is focused on the analysis of secondary data, it does not require ethics approval. The results of the study will be disseminated through articles in peer-reviewed journals and trade publications as well as presentations at relevant conferences.

PROTOCOL REGISTRATION: International Prospective Register for Systematic Reviews (PROSPERO) number CRD42017068164.

KEYWORDS: systematic review - chemotherapy -Hospitalization At Home- cancer care -Costs -Home Care - Quality Of Life

STRENGHTS AND LIMITATIONS OF THIS STUDY:

- This will be one of the first attempts to synthesize and critically appraise the current state of evidence about the comparison between home setting and hospital setting for the parenteral chemotherapy administration in the same high standards of clinical care. The systematic review protocol is developed using the Preferred Reporting Items for Systematic Reviews and meta-analyses for Protocols (PRISMA-P) guidelines and includes the search to literature published in two languages and the wide search from published studies to the grey literature.

- Methodological quality of studies will be assessed using the "Quality Assessment Tool for Quantitative Studies" developed by the Effective Public Health Practice Project (EPHHP) tool in addition to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement for economic studies.

- Based on previous work, we anticipate methodological heterogeneity and statistical heterogeneity leading to difficulty to analyze data quantitatively.

- The definition of home-based services is confusing including different types of interventions leading to discrepancies when analyzing.

INTRODUCTION

Hospital remains the main setting for parenteral cancer chemotherapy administration despite the patient's general positive feeling about receiving care at home,[1]. As the worldwide incidence of cancers increases,[2] and, bearing in mind that due to progress in efficacy of treatments, cancer is becoming a long-term disease, along with advances in diagnostic technology and novel targeted treatments, with their financial constraints, it is necessary to develop alternative models of health service delivery such as home programs, without detrimental effects on health outcomes and costs. Despite the feasibility,[3-5] and despite policies to enable more to receive chemotherapy at home, in a few countries,[6,7], the parenteral chemotherapy administration at home remains marginal due to little evidence, for improving the health outcomes, for patient's quality of life and for cost savings. Furthermore, findings on outcomes varied leading sometimes to conflicting results,[8-10]. A recent scoping study demonstrates most economic studies concluded in favor of home care, but according to the appropriate type, all sources of expenditure (specialized clinical care, transportation, out-of-pocket expenses, etc…) were not systematically assessed,[11,12] whereas other studies showed no significant difference in the overall costs,[9,10]. Likewise, the impacts on caregivers especially the shift of the care burden from hospital to relatives have rarely been studied. To date, only one existing review of home-based chemotherapy,[13] and it ended in favor of administration at home but, this conclusion is hampered by a mix between routes of administration (parenteral and oral intake) and type of care (administration and post administration follow-up).

Considering these facts, a systematic review will be undertaken for providing a complete overview of parenteral cancer chemotherapy administration at home to investigate whether the clinical outcomes are maintained and the resources utilization are reduced in comparison to hospital high standard care.

METHODS:

This protocol has been prepared following the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (P-PRISMA) approach,[14] to increase the confidence in the findings. It has been registered in International Prospective Register of Systematic Reviews database (no CRD42017068164).

Types of studies

Except the crossover studies, all types of studies that have investigated the parenteral cancer chemotherapy home administration compared to hospital setting as randomized, controlled or uncontrolled trials, cohort studies, and, parallel studies will be included if they fulfill at least one of the following criteria:

1) Assessment of the impact of parenteral chemotherapy administration on patients' health outcomes, whatever they are: survival, relapse, tolerance

2) Assessment of the impact of parenteral chemotherapy administration on patients 'or caregivers 'satisfaction

3) Assessment of the impact of parenteral chemotherapy administration on cost savings

4) Assessment of the incentives and/or the barriers according to the patients and/or relatives' point of view

The economic evaluations about the resources utilization with the costs and consequences such as cost-effectiveness, cost-utility or cost-benefit, either without any clinical assessment, will be included.

The crossover studies will be excluded from the review: the crossover studies involving oncology products or the type of hospitalization setting, could suffer from order effects, so that, it could be difficult to confirm statistically the lack of order effects and hence, to use the results.

Participants:

We will be interested in studies on participants receiving parenteral anti-cancer drug administration at home compared to patients receiving the drugs in a hospital setting. There will be no restriction concerning the type of tumor disease, age or sex of participants.

Eligibility criteria

All studies exploring parenteral anti-cancer drug administration at home setting, mainly intravenous and subcutaneous administration, will be selected from the earliest available data through November 15th, 2017 published in French and English languages, whatever the country. The inclusion criteria defining the scope of publications included in the review will be the comparison of parenteral chemotherapy administration at home with administration in-patients and/or out-patients wards.

As our goal is to study the home-based setting as an alternative context for providing the highest standards of clinical care concerning the parenteral drug delivery, we will exclude all community-based services with no anti-cancer drugs administration at home and the studies targeting only the post-administration chemotherapy monitoring, the disconnection of portable diffusor, the management of central venous catheter, and the supportive care therapy. For the same reasons, studies about oral anticancer drugs will be excluded as the oral treatment does not require hospital care, patients usually manage their pills themselves with an ambulatory follow-up and the treatment issues are deeply different (i.e chronic side effects, patient's compliance).

Databases and Search strategy:

A detailed literature search will be conducted to identify all articles studying chemotherapy administration in home setting for adults and pediatrics patients. Published studies will be identified through searches of the Medline, Cochrane, Web of Science databases, Embase and Cumulative Index of Nursing and Allied Health (Cinahl) from the earliest available date through November 15th, 2017. HAH is defined as the delivery of hospital ward level care and replaces hospital by ensuring the continuity of care for the patients it takes care of. HAH is also known as “hospital in the home”, “home hospitalization” and “early supported discharge”,[15-17]. The MeSH definition of “Home Care Services” is defined as a community health and nursing services providing coordinated multiple services to the patient at the patient's homes. These home care services are provided by a visiting nurse, home health agencies, hospitals, or organized community groups using professional staff for care delivery. It differs from home nursing which is provided by non-professionals and, of “Home Care Agencies”, public or private organizations that provide, either directly or through arrangements with other organizations, home health services in the patient's home.

Therefore, we have developed a strategy in Medline to retrieve relevant literature on the topic. The MEDLINE search strategy will be ("Neoplasms"[Mesh] AND ("Antineoplastic Combined Chemotherapy Protocols"[Mesh] OR "Antineoplastic Agents"[Mesh])) AND ("Home Care Services"[Mesh] OR "Home Care Agencies"[Mesh]). This search strategy will be adapted in searching other databases. The references from potentially relevant papers were manually searched for additional studies. A further research will be performed in Opengrey, in Research papers in Economics (RePec) and in Google Scholar databases to find relevant unpublished studies in grey literature.

Study selection:

We will use a two-stage process for the identification of papers that met our inclusion criteria. The first stage accumulated all papers from the two types of searches using the already mentioned databases. The first type of search will use combinations of keywords to retrieve titles of potentially relevant studies. The search output will be screened independently by two review authors (MDS, BMM) to identify studies that potentially meet the inclusion criteria outlined above. In case of discrepancy, the abstract of the concerned study will be retrieved. If disagreements are remained, a third author (EB) will arbitrate. In the second type of search, all papers citing or cited by articles that had already met our inclusion criteria will be identified then screened as the first ones. In the second stage, the full text of these selected studies will be retrieved and independently assessed for eligibility by the same two review members. An article will be considered relevant and kept for analysis if the full text for the publication will be a comparison design assessing patient’s health or/and safety outcomes or/and patients’ or relatives satisfaction, or/and cost-savings

or/and the incentives and the barriers of using home as an alternative setting. The duplicates of articles will be discarded.

Any disagreement between them over the eligibility of particular studies will be resolved through discussion with a 3rd reviewer (EB).

Data extraction

Extracted information to a standardized form will include:

- study setting

- study population

- tumor type and chemotherapy regimen

- details of the intervention/control conditions

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- patients' health outcomes including Quality of Life, duration of survival, progression of disease, toxicity

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- Incentives and barriers according to the patients' and/or relatives' point of view

- Information for the assessment of the risk of bias

Data will be extracted independently by the two review members; discrepancies will be identified and resolved through discussion with a 3rd reviewer (PA).

Data assessment and synthesis:

Quality assessment

Two reviewers (MDS and BMM) will independently assess the quality of included studies and the potential risk of bias. We will use the "Quality Assessment Tool for Quantitative Studies" developed by the Effective

Public Health Practice Project (EPHHP) tool,[18] as it can be applied to articles of any public health topic area , assessing the components of studies (design, methods, bias). Likewise, we will use the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement,[19], focusing on the design quality of the costs studies. It is leading to an overall methodological rating of strong, moderate or weak. Consensus will be reached through discussion in case of disagreement.

Data synthesis

According to the limited development of home parenteral chemotherapy administration, we anticipate methodological heterogeneity, statistical heterogeneity, heterogeneity of the interventions and, heterogeneity of the models against a meta-analysis of the evidence base. In that case, an interpretative method should be more appropriate leading to the description of the observed effects with peculiarities, strengths and, limits of each study, according to the quality of the study, to the type of study, to the studied population and, to the interventions. This method should be more appropriate from a holistic point of view.

Subgroup analysis

If the data are available, we will conduct subgroup analyses investigating the effects of the study design, the models, the interventions, the effect of the tumor type (hematologic tumor, solid tumor) and, the effects of the age of the study population (children, young people < 18 years old, adults, > 65 years old).

A sensitivity analysis will determine the robustness of the observed outcomes facing publication language, clinical or methodological heterogeneity.

Ethics and dissemination: As the review is focused on the analysis of secondary data, it does not require ethics approval. The results of the study will be disseminated through articles in peer-reviewed journals and trade publications as well as presentations at relevant conferences.

CONCLUSION

This review will be an attempt to synthesize and to critically appraise the impact on parenteral chemotherapy administration at home for the patients and their relatives compared to the hospital setting and, following the P-PRISMA guidelines.

Others strengths of this review include the search to literature published in two languages, French and English and the wide search from published studies to the grey literature.

It is although, acknowledged that the definition of home-based services is confusing including different types of interventions and could lead to discrepancies when analyzing. Likewise, the results of the review may be limited by the diversity of the study designs and present challenges in the quality assessment. These limitations will be considered in relation to the review findings.

However, this review could be useful for the medical staffs to choice the best treatment setting for patients and their relatives, contributes to develop the parenteral chemotherapy administration at home and highlights to define the realistic methodology to set up in this field.

Contributors: All authors made substantive intellectual contributions to the development of this protocol. BMM wrote this protocol. MDS, EB, PA commented critically the manuscript and involved in conceptualizing the review. JA commented critically the manuscript.

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Impacts on health outcomes and on resources utilization for home based parenteral chemotherapy administration: a systematic review protocol

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ABSTRACT

INTRODUCTION:

Despite policies, in a few countries, to enable more to receive chemotherapy at home and despite the demonstrated feasibility, the parenteral chemotherapy administration at home remains currently marginal. Of note, findings of different studies on health outcomes and resources utilization vary leading to conflicting results. This protocol outlines a systematic review that seeks to synthesize and critically appraise the current state of evidence about the comparison between home setting and hospital setting for the parenteral chemotherapy administration within the same high standards of clinical care.

METHODS AND ANALYSIS:

This protocol has been prepared following the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (P-PRISMA) approach. Electronic searches will be conducted on bibliographic databases selected from the earliest available data through November 15th, 2017 published in French and English languages. Additional potential papers in the selected studies and grey literature will be also included in the review. The review will include all types of studies exploring patients receiving anti-cancer drug for injection at home compared to patients receiving the drugs in hospital setting and will assess at least one of the following criteria: the patients' health outcomes, the patients 'or caregivers 'satisfaction, the resources utilization with cost savings, the incentives and/or the barriers of each admission setting according to the patients and relatives' point of view. Two reviewers will independently screen studies and extract relevant data from included studies. Methodological quality of studies will be assessed using the "Quality Assessment Tool for Quantitative Studies" developed by the Effective Public Health Practice Project (EPHHP) tool in addition to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement for economic studies.

ETHICS AND DISSEMINATION: As the review is focused on the analysis of secondary data, it does not require ethics approval. The results of the study will be disseminated through articles in peer-reviewed journals and trade publications as well as presentations at relevant conferences.

PROTOCOL REGISTRATION: International Prospective Register for Systematic Reviews (PROSPERO) number CRD42017068164.

KEYWORDS: Chemotherapy - Public Health - Organization of health services – Health economics – Hospital At Home

STRENGHTS AND LIMITATIONS OF THIS STUDY:

- This will be one of the first attempts to synthesize and critically appraise the current state of evidence about the comparison between home setting and hospital setting for the parenteral chemotherapy administration.
- The systematic review protocol is developed using the Preferred Reporting Items for Systematic Reviews and meta-analyses for Protocols (PRISMA-P) guidelines.
- Based on previous work, we anticipate methodological heterogeneity and statistical heterogeneity leading to difficulty to analyze data quantitatively.
- The definition of home-based services is confusing including different types of interventions leading to discrepancies when analyzing.

INTRODUCTION

Hospital remains the main setting for parenteral cancer chemotherapy administration despite the patient's general positive feeling about receiving care at home,[1]. As the worldwide incidence of cancers increases,[2] and, bearing in mind that due to progress in efficacy of treatments, cancer is becoming a long-term disease, along with advances in diagnostic technology and novel targeted treatments, with their financial constraints, it is necessary to develop alternative models of health service delivery such as home programs, without detrimental effects on health outcomes and costs. Despite the feasibility,[3-5] and despite policies to enable more to receive chemotherapy at home, in a few countries,[6,7], the parenteral chemotherapy administration at home remains marginal due to little evidence, for improving the health outcomes, for patient's quality of life and for cost savings. Furthermore, findings on outcomes varied leading sometimes to conflicting results,[8-10]. A recent scoping study demonstrates most economic studies concluded in favor of home care, but according to the appropriate type, all sources of expenditure (specialized clinical care, transportation, out-of-pocket expenses, etc…) were not systematically assessed,[11,12] whereas other studies showed no significant difference in the overall costs,[9,10]. Likewise, the impacts on caregivers especially the shift of the care burden from hospital to relatives have rarely been studied. To date, only one existing review of home-based chemotherapy,[13] and it ended in favor of administration at home but, this conclusion is hampered by a mix between routes of administration (parenteral and oral intake) and type of care (administration and post administration follow-up).

Considering these facts, a systematic review will be undertaken for providing a complete overview of parenteral cancer chemotherapy administration at home to investigate whether the clinical outcomes are maintained and the resources utilization are reduced in comparison to hospital high standard care.

METHODS:

This protocol has been prepared following the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (P-PRISMA) approach,[14] to increase the confidence in the findings. It has been registered in International Prospective Register of Systematic Reviews database (no CRD42017068164).

Types of studies

Except the crossover studies, all types of studies that have investigated the parenteral cancer chemotherapy home administration compared to hospital setting as randomized, controlled or uncontrolled trials, cohort studies, and, parallel studies will be included if they fulfill at least one of the following criteria:

1) Assessment of the impact of parenteral chemotherapy administration on patients' health outcomes, whatever they are: survival, relapse, tolerance

2) Assessment of the impact of parenteral chemotherapy administration on patients 'or caregivers 'satisfaction

3) Assessment of the impact of parenteral chemotherapy administration on cost savings

4) Assessment of the incentives and/or the barriers according to the patients and/or relatives' point of view

The economic evaluations about the resources utilization with the costs and consequences such as cost-effectiveness, cost-utility or cost-benefit, either without any clinical assessment, will be included.

The crossover studies will be excluded from the review: the crossover studies involving oncology products or the type of hospitalization setting, could suffer from order effects, so that, it could be difficult to confirm statistically the lack of order effects and hence, to use the results.

Participants:

We will be interested in studies on participants receiving parenteral anti-cancer drug administration at home compared to patients receiving the drugs in a hospital setting. There will be no restriction concerning the type of tumor disease, age or sex of participants.

Patients and Public Involvement

As the review is focused on the analysis of secondary data, it does not involve patients nor for the design of the study neither for the dissemination of the results.

Eligibility criteria

All studies exploring parenteral anti-cancer drug administration at home setting, mainly intravenous and subcutaneous administration, will be selected from the earliest available data through November 15th, 2017 published in French and English languages, whatever the country. The inclusion criteria defining the scope of publications included in the review will be the comparison of parenteral chemotherapy administration at home with administration in-patients and/or out-patients wards. As our goal is to study the home-based setting as an alternative context for providing the highest standards of clinical care concerning the

parenteral drug delivery, we will exclude all community-based services with no anti-cancer drugs administration at home and the studies targeting only the post-administration chemotherapy monitoring, the disconnection of portable diffusor, the management of central venous catheter, and the supportive care therapy. For the same reasons, studies about oral anticancer drugs will be excluded as the oral treatment does not require hospital care, patients usually manage their pills themselves with an ambulatory follow-up and the treatment issues are deeply different (i.e chronic side effects, patient's compliance).

Databases and Search strategy:

A detailed literature search will be conducted to identify all articles studying chemotherapy administration in home setting for adults and pediatrics patients. Published studies will be identified through searches of the Medline, Cochrane, Web of Science databases, Embase and Cumulative Index of Nursing and Allied Health (Cinahl) from the earliest available date through November 15th, 2017. HAH is defined as the delivery of hospital ward level care and replaces hospital by ensuring the continuity of care for the patients it takes care of. HAH is also known as "hospital in the home", "home hospitalization" and "early supported discharge",[15-17]. The MeSH definition of "Home Care Services" is defined as a community health and nursing services providing coordinated multiple services to the patient at the patient's homes. These home care services are provided by a visiting nurse, home health agencies, hospitals, or organized community groups using professional staff for care delivery. It differs from home nursing which is provided by non-professionals and, of "Home Care Agencies", public or private organizations that provide, either directly or through arrangements with other organizations, home health services in the patient's home.

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According to the limited development of home parenteral chemotherapy administration, we anticipate methodological heterogeneity, statistical heterogeneity, heterogeneity of the interventions and, heterogeneity of the models against a meta-analysis of the evidence base. In that case, an interpretative method should be more appropriate leading to the description of the observed effects with peculiarities, strengths and, limits of each study, according to the quality of the study, to the type of study, to the studied population and, to the interventions. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach,[20], will be used to assess the overall quality of evidence by downgrading scores in case of serious risk of bias, of imprecision, of study limitations, or indeed, by upgrading scores for studies what traditionally has been considered as a weak design. It would be appropriate to assess relevant studies which are not provide evidence regarding every outcome. Final scores for the quality of evidence will be categorised as high, moderate, low or very low and summarised in table. This method should be more appropriate from a holistic point of view.

Subgroup analysis

If the data are available, we will conduct subgroup analyses investigating the effects of the study design, the models, the interventions, the effect of the tumor type (hematologic tumor, solid tumor) and, the effects of the age of the study population (children, young people < 18 years old, adults, > 65 years old).

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Search strategy and key words used :

1. **Antineoplastic agents** OR **Chemotherapy**

2. **Home Care** OR **Hospital At Home** OR **Home Care Services** OR **Home Infusion Therapy**

3. **Injection** OR **Infusion** OR **Perfusion** OR **Parenteral** OR **Intravenous** OR **Subcutaneous**

4. 1 AND 2 AND 3

5. ("Neoplasms"[Mesh] AND ("Antineoplastic Combined Chemotherapy Protocols"[Mesh] OR "Antineoplastic Agents"[Mesh])) AND ("Home Care Services"[Mesh] OR "Home Care Agencies"[Mesh])

6. **Injection** AND **'Home care'** AND **'Chemotherapy'**