Author's response to reviews

Title: Scaling up depot medroxyprogesterone acetate (DMPA): A systematic literature review illustrating the AIDED model

Authors:

Leslie Curry (leslie.curry@yale.edu)
Elizabeth H Bradley (elizabeth.bradley@yale.edu)
Lauren Taylor (laurenannetaylor@gmail.com)
Emily Cherlin (emily.cherlin@yale.edu)
Sarah W Pallas (sarah.pallas@yale.edu)
Kristina Talbert-Slagle (kristina.talbert-slagle@yale.edu)
Christina T Yuan (christina.yuan@yale.edu)
Dana K Ciccone (dana.ciccone@yale.edu)
Rafael Pérez-Escamilla (rafael.perez-escamilla@yale.edu)

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Author's response to reviews: see over
25 July 2013

Dr. Jose Belizan
Editor-in-Chief
Reproductive Health

Dear Dr. Belizan:

Thank you for your continued review of our paper, “Depo-Provera: An Application of the AIDED Model,” which we have retitled, “Scaling up depotmedroxyprogesterone acetate (DMPA): A systematic literature review illustrating the AIDED model.” We have read the comments from the reviewers and have included an itemized list of each comment and our response with this letter of resubmission. The revisions to the manuscript have been recorded in track changes.

We believe the paper has been much improved through the review process and appreciate the time and effort you have devoted to our work. We look forward to your continued review; please let me know if you have any questions.

Sincerely,

Leslie Curry, PhD, MPH
Senior Research Scientist and Lecturer in Public Health
Co-Director, Robert Wood Johnson Clinical Scholars Program
REVIEWER 1 (ELENA LEBETKIN) COMMENTS AND AUTHORS’ RESPONSES

Note: page numbers in author responses refer to revised manuscript with track changes edits accepted.

Major Compulsory Revisions

Comment #1
The authors do not exhibit a sufficient understanding and knowledge of the literature on community based distribution of DMPA to appropriately investigate the application of the AIDED model. Please see the comments below for clarification.

Response
Thank you for your feedback. We have substantially revised the Background section to better demonstrate our knowledge of the literature on depot medroxyprogesterone acetate (DMPA). We have also sought to clarify that our focus was specifically on DMPA, rather than injectable contraceptives more generally (a focus which may have resulted in the exclusion of some sources that only discuss injectable contraceptives in general terms rather than DMPA specifically), and, importantly, on scaling up DMPA as a contraceptive product rather than scaling up community-based distribution of DMPA as a delivery method. The revised Background section (the majority of which is new text in response to Reviewer 2’s recommendation to provide further background about the AIDED model) is excerpted below (in particular, see underlined text):

Background (Pp. 3-4): A puzzle in reproductive health, and public health generally, has long been why innovative products and programs spread widely and rapidly in some contexts but fail to spread in others. Multiple models of spread focus on active dissemination of an innovation, providing recommendations for how to facilitate or accelerate take up [1-5], while other models have described the process of passive diffusion of innovations [6-8]. In work described elsewhere [9], our team identified characteristics associated with successful innovation spread – encompassing both active dissemination and passive diffusion – and developed a new model to capture these dynamics in the domain of family health. The resulting nonlinear, complex adaptive system model, called AIDED (Figure 1), was designed for flexible application across diverse innovation types, including products, behaviors, organizational structures, and delivery systems. The AIDED model thus differs from prior models of reproductive health intervention scale up in that it applies to a broader range of innovations and incorporates both active dissemination and passive diffusion processes, fully recognizing the complex adaptive system nature of scaling up processes.

The description of the AIDED model [9] has consisted of a synthesis of findings across a range of innovation types and may be of use to providers and policymakers interested in family health innovations broadly. However, the current descriptions may be of limited use to those interested in ‘products’ such as injectable contraceptives. This paper provides an in-depth illustration of the AIDED model using results from a systematic review of the academic and grey literature about dissemination, diffusion, scale up, and sustainability of depot medroxyprogesterone acetate (DMPA). DMPA, often known by the brand name Depo-Provera, is a long-acting contraceptive administered by intramuscular injection that is an effective, convenient, reversible, and increasingly popular family planning method [10-14]. Recognition of these benefits, accompanied by approval by the U.S. Food and Drug Administration in 1992, catalyzed a global doubling of injectable contraceptive use between 1995 and 2005, a trend that was particularly prevalent among low-income countries [15]. DMPA scale up has been described in several countries including Bangladesh [16], Uganda [17], Ghana [15], Vietnam [18, 19], Taiwan [20], Afghanistan [21], Malawi [22], India [23] and Zimbabwe (Rhodesia) [24]. As a
well-documented reproductive health technology that has scaled up in diverse contexts, DMPA offers an exemplar “product-type” innovation in the domain of family health for illustrating the AIDED model’s usefulness. We selected DMPA rather than other injectable contraceptives on account of its longer duration, which is a distinguishing feature that is advantageous in settings where access to health care is difficult; DMPA is also the most prevalent injectable contraceptive used globally [15, 25].

Previous literature about scaling up DMPA has tended to focus on the distribution channel, such as whether clinic-based or community-based distribution is used. Numerous findings related to the safety and efficacy of community-based distribution (CBD) of DMPA have been published [10-12, 14, 23, 26-29] and recently synthesized [11] and toolkits to aid policy makers and practitioners in scaling up community-based access to injectables have also been produced [30-33]. By contrast, this paper seeks to synthesize evidence about the enabling factors and barriers to scale up of DMPA as a product, rather than scale up of a particular DMPA distribution channel. Our focus is therefore on cases in which DMPA use has spread from a smaller number to a larger number of user groups, regardless of whether that spread occurred via clinic-based or community-based approaches. In this paper we map the evidence about DMPA scale up to the AIDED model, summarizing relevant peer-reviewed and grey literature to illustrate the model with a specific product innovation, and identify lessons for scaling up of DMPA and other contraceptive technologies in low- and middle-income countries.

Comment #2
Background, paragraph 1: You discuss community-based models of distribution throughout the paper. This is confusing as you are discussing applying the AIDED model for scale-up. It would make more sense if you referred to the community-based distribution of DMPA as just CBD of DMPA and then discussed how your sources followed the AIDED model.

Response
Thank you for this suggestion. We have revised the language throughout the manuscript so that we refer to the community-based distribution (CBD) of DMPA as just “CBD of DMPA” and discuss how our sources followed the AIDED model.

Comment #3
Background, paragraph 2: I disagree with the author’s assessment that little is known about the process of moving from implementation to scaling up models of CBD of DMPA. There is a large body of literature (both peer reviewed and gray) that addresses the scale up of CBD of DMPA. There is a K4Health toolkit on community based access to injectables (CBA2I) that has extensive documentation - http://www.k4health.org/toolkits/cba2i. The page on scale-up (http://www.k4health.org/toolkits/cba2i/scale) has a link to resources on how to scale up as well as examples of successful scale up. Some of these sources were cited by the authors, others were not. I would particularly recommend the authors look at the annotated bibliography (http://www.k4health.org/toolkits/cba2i/scaling-annotated-bibliography) on this website for additional publications that describe the scale-up of CBA2I.

Response
We appreciate your comments about the extent of the existing literature on scaling up community-based distribution of injectable contraceptives. As part of our study, we had reviewed the documentation available from K4Health, including the sources noted in the annotated bibliography. We have revised the Background section to better reflect the state of the existing literature and the
contribution of our manuscript. We have also added further citations, including from the K4Health annotated bibliography, to provide a more comprehensive indication of the available literature; please refer to the end of this letter for a revised reference list, which indicates the new references that we have added. As recommended, we have deleted the sentence from the original manuscript that stated that “little is known about the process of moving from implementation to scaling up of community-based distribution of Depo-Provera.” We have added the following to the manuscript:

Background (P. 4, new text): Previous literature about scaling up DMPA has tended to focus on the distribution channel, such as whether clinic-based or community-based distribution is used. Numerous findings related to the safety and efficacy of community-based distribution (CBD) of DMPA have been published [10-12, 14, 23, 26-29] and recently synthesized [11] and toolkits to aid policy makers and practitioners in scaling up community-based access to injectables have also been produced [30-33]. By contrast, this paper seeks to synthesize evidence about the enabling factors and barriers to scale up of DMPA as a product, rather than scale up of a particular DMPA distribution channel. Our focus is therefore on cases in which DMPA use has spread from a smaller number to a larger number of user groups, regardless of whether that spread occurred via clinic-based or community-based approaches. In this paper we map the evidence about DMPA scale up to the AIDED model, summarizing relevant peer-reviewed and grey literature to illustrate the model with a specific product innovation, and identify lessons for scaling up of DMPA and other contraceptive technologies in low- and middle-income countries.

Comment #4
Background, paragraph 2: Bangladesh is not included in the list of countries that have documented scale-up. The work of ICDDR,B on the Matlab Project is very well documented in the literature and is regularly cited as the first documented case of not only CBD of DMPA, but also scaling up CBD of DMPA.

Response
Thank you for noting the importance of the Bangladesh case. The list of countries in the Background, paragraph 2, was intended to be illustrative rather than comprehensive. We have added Bangladesh to this list so that the sentence now reads (P. 4, edit underlined):

DMPA scale up has been described in several countries including Bangladesh [16], Uganda [17], Ghana [15], Vietnam [18, 19], Taiwan [20], Afghanistan [21], Malawi [22], India [23] and Zimbabwe (Rhodesia) [24].

Comment #5
Background, paragraph 4: I disagree with the author’s statement that “none of the existing frameworks have proposed a theory of the interrelated actions important for scale up”. The authors cite ExpandNet (reference 16) as one of the models. ExpandNet’s own materials state: “Scaling up is portrayed as an open system of five elements that interact with one another: the innovation, the user organization, the environment, the resource team or organization and the scaling up strategy” (http://www.expandnet.net/PDFs/WHO_ExpandNet_Practical_Guide_published.pdf).

Response
Thank you for highlighting the ExpandNet framework. We view the ExpandNet framework as presenting a model of five discrete elements rather than five interrelated actions; by comparison, the AIDED model presents five actions, or processes, that characterize successful scale up (assess, innovate, develop, engage, and devolve). Although we refer to the parts of the AIDED model as “components” in the
manuscript for ease of exposition, each component is in fact a process. We acknowledge that the ExpandNet framework is presented along with a nine-step “process of formulating a scaling-up strategy” (ExpandNet/WHO 2009, p. 7); however, we see this process as separate from the framework itself and as highly linear in nature. By contrast, the AIDED model is nonlinear in nature, emphasizing that the five actions of the model may not proceed sequentially, that feedback loops exist among the five actions, and that scale up occurs within a complex adaptive system with several possible paths for achieving widespread innovation use.

We have revised the Background section per your comments and those of Reviewer 2 to more clearly highlight the distinctive aspects of the AIDED model and our aim in using DMPA to illustrate the model. We have also added a new section following the Background that summarizes the AIDED model. This new AIDED Model section compiles in a single location at the beginning of the manuscript the descriptions of the 5 AIDED components that had been interspersed in the Results section in the original manuscript. The relevant revised sections are excerpted below:

**Background (P. 3, new text):** A puzzle in reproductive health, and public health generally, has long been why innovative products and programs spread widely and rapidly in some contexts but fail to spread in others. Multiple models of spread focus on active dissemination of an innovation, providing recommendations for how to facilitate or accelerate take up [1-5], while other models have described the process of passive diffusion of innovations [6-8]. In work described elsewhere [9], our team identified characteristics associated with successful innovation spread – encompassing both active dissemination and passive diffusion – and developed a new model to capture these dynamics in the domain of family health. The resulting nonlinear, complex adaptive system model, called AIDED (Figure 1), was designed for flexible application across diverse innovation types, including products, behaviors, organizational structures, and delivery systems. The AIDED model thus differs from prior models of reproductive health intervention scale up in that it applies to a broader range of innovations and incorporates both active dissemination and passive diffusion processes, fully recognizing the complex adaptive system nature of scaling up processes.

**The AIDED Model (Pp. 4-6):** The AIDED model includes 5 non-linear, interrelated components: 1) assess the landscape, 2) innovate to fit user receptivity, 3) develop support, 4) engage user groups, and 5) devolve efforts for spreading innovation [9]. Each component captures a set of processes; this action-based approach distinguishes the AIDED model from other scale up frameworks that focus on actors or context [2-4, 6, 34]. The model suggests that successful scale up occurs within a complex adaptive system, characterized by interdependent parts, multiple feedback loops, and several potential paths to achieve intended outcomes. The AIDED model’s nonlinear nature is another distinctive feature relative to existing approaches to scale up strategy design [1, 35]. Importantly, the AIDED model was developed with groups (e.g., organization or community) as its unit of analysis and mechanism of spread, in contrast to prior scale-up studies of individual behavior change [36-38].

The ASSESS component refers to assessment of the broad landscape within a potential user group, including the needs and wants of the user community, its absorptive capacity, and the political, economic, legal/regulatory, technological and social conditions within its internal and external environment. The INNOVATE component includes designing, re-designing, and packaging an innovation so that the innovation is acceptable and perceived as advantageous by potential user groups in their specific context or environment. These processes of designing, re-designing, and packaging the innovation are aimed at achieving ‘fit’ between the innovation and
the user group. In the DEVELOP component, attention is directed to fostering enabling relationships, environments and networks among partners that can support and facilitate spread of the innovation. Although engagement occurs throughout the process of dissemination and diffusion, the ENGAGE component involves the specific tasks of introducing the innovation from outside the user group to inside the user group, translating the innovation so that user groups can assimilate the new information, and integrating the innovation into the routine practices and social norms of the user group. Finally, the DEVOLVE component involves the initial user groups releasing and spreading the innovation for its re-introduction in new user groups within their peer networks. These user groups and their networks replicate and release the innovation (in adapted and potentially failed forms) in the way they see most appropriate.

The AIDED model is both descriptive of common features of successful innovation spread, and prescriptive of processes that should be considered by those wishing to facilitate scale up.

Comment #6
Methods, paragraph 3: Clinic-based and community-based services are very different especially when it comes to scale-up as the staff, supply chain, supervision, delivery, and other factors are totally different. As this article is focused on CBD of DMPA, please remove any clinic-based scale-up articles.

Response
We recognize and agree that there is an important distinction between clinic-based and community-based services. We have revised the Background section to clarify that the focus of our study was on scale up of DMPA as a contraceptive product, rather than scale up of community-based distribution of DMPA:

Background (p. 4, new text): Previous literature about scaling up DMPA has tended to focus on the distribution channel, such as whether clinic-based or community-based distribution is used. Numerous findings related to the safety and efficacy of community-based distribution (CBD) of DMPA have been published [10-12, 14, 23, 26-29] and recently synthesized [11] and toolkits to aid policy makers and practitioners in scaling up community-based access to injectables have also been produced [30-33]. By contrast, this paper seeks to synthesize evidence about the enabling factors and barriers to scale up of DMPA as a contraceptive product, rather than scale up of a particular DMPA distribution channel. Our focus is therefore on cases in which DMPA use has spread from a smaller number to a larger number of user groups, regardless of whether that spread occurred via clinic-based or community-based approaches. In this paper we map the evidence about DMPA scale up to the AIDED model, summarizing relevant peer-reviewed and grey literature to illustrate the model with a specific product innovation, and identify lessons for scaling up of DMPA and other contraceptive technologies in low- and middle-income countries.

As we are considering scale up of the product rather than scale up of a delivery approach, we included literature that described either clinic-based or community-based distribution. We have clarified the language in paragraph 3 of the Methods section as follows:

Methods (P. 8, edit underlined): While some characteristics relevant to scale up differ between clinic-based provision and CBD of DMPA, as our focus was on DMPA as a product innovation rather than on scaling up a specific delivery method, we chose to include both delivery methods in this review in order to identify common elements and extract as much information as possible from the limited published literature.
**Minor Essential Revisions**

Comment #7

Depo Provera is the brand name of the drug. Please refer to it as depot medroxyprogesterone acetate (DMPA).

Response

We have changed references to Depo-Provera throughout the manuscript to DMPA. We have retained references to Depo-Provera in the Abstract and the Introduction to facilitate retrieval by readers who may search for articles related to Depo-Provera, highlighting that this is the brand name (see underlined text):

**Abstract (P. 2):** Use of depot medroxyprogesterone acetate (DMPA), often known by the brand name Depo-Provera, has increased globally, particularly in multiple low- and middle-income countries (LMICs).

**Introduction (P. 3):** DMPA, often known by the brand name Depo-Provera, is a long-acting contraceptive administered by intramuscular injection that is an effective, convenient, reversible, and increasingly popular family planning method [10-14].

Depo-Provera is also mentioned in the Methods section among the search terms used in our systematic review (P. 6) and in the Results section when citing a study that specifically referred to the brand name product (P. 14).

Comment #8

Background, paragraph 1: The statement “the availability of any form of contraception, is novel” is too broad. You would be hard pressed to find a community that has no access to any form of contraception especially if you consider natural family planning methods.

Response

Thank you for your comment. We have deleted this sentence in our revision of the Background section.

Comment #9

Results, Assess section, Illustrative example paragraph: It’s called a “situation analysis” not “situational analysis”.

Response

We used the term “situational analysis” because this is the term that was used to describe the activity in the original source (Fajans et al 2007, pp. 35, 40, 41). As both situation analysis and situational analysis are regularly used in peer-reviewed literature, we do not feel that retaining “situational analysis” will impede the reader’s comprehension and doing so will be faithful to the original source. We have therefore left the term as is but we defer to the editor on this.

**Discretionary Revisions**

Comment #10

While I realize that the article 14 cited (Kaler A.) refers to Zimbabwe as Rhodesia, I would recommend referring to the country with the current name in your publication and putting Rhodesia in parentheses.
Response
Thank you for this suggestion. We have revised references to Rhodesia throughout the manuscript to read “Zimbabwe (Rhodesia).”

WORKS CITED IN AUTHOR RESPONSES
Please see end of letter for list of references in text excerpted from revised manuscript.


Major Compulsory Revisions
Comment #1
The paper seems to “bury the lead”. The background and abstract sections begin and spend a great deal of time describing CBD of DMPA. However, I believe the paper and the systematic review is intended to focus on the validation of the AIDED model. It seems to me the paper needs to invert the background section beginning with a discussion of AIDED and its relationship to other scale-up frameworks with more discussion of what the 5 components of the AIDED framework mean.

Response
Thank you for this helpful feedback. We have substantially revised the Background section as recommended to begin with the AIDED model and then explain that we are using DMPA as an example of a product innovation to illustrate the model. We have also added a new section after the Background to summarize the AIDED model. This new AIDED Model section compiles in a single location at the beginning of the manuscript the descriptions of the 5 AIDED components that had been interspersed in the Results section in the original manuscript. The revised Background and AIDED Model sections are excerpted below:

Background (Pp. 3-4): A puzzle in reproductive health, and public health generally, has long been why innovative products and programs spread widely and rapidly in some contexts but fail to spread in others. Multiple models of spread focus on active dissemination of an innovation, providing recommendations for how to facilitate or accelerate take up [1-5], while other models have described the process of passive diffusion of innovations [6-8]. In work described elsewhere [9], our team identified characteristics associated with successful innovation spread – encompassing both active dissemination and passive diffusion – and developed a new model to capture these dynamics in the domain of family health. The resulting nonlinear, complex adaptive system model, called AIDED (Figure 1), was designed for flexible application across diverse innovation types, including products, behaviors, organizational structures, and delivery systems. The AIDED model thus differs from prior models of reproductive health intervention scale up in that it applies to a broader range of innovations and incorporates both active dissemination and passive diffusion processes, fully recognizing the complex adaptive system nature of scaling up processes.

The description of the AIDED model [9] has consisted of a synthesis of findings across a range of innovation types and may be of use to providers and policymakers interested in family health innovations broadly. However, the current descriptions may be of limited use to those interested in ‘products’ such as injectable contraceptives. This paper provides an in-depth illustration of the AIDED model using results from a systematic review of the academic and grey literature about dissemination, diffusion, scale up, and sustainability of depot medroxyprogesterone acetate (DMPA). DMPA, often known by the brand name Depo-Provera, is a long-acting contraceptive administered by intramuscular injection that is an effective, convenient, reversible, and increasingly popular family planning method [10-14]. Recognition of these benefits, accompanied by approval by the U.S. Food and Drug Administration in 1992, catalyzed a global doubling of injectable contraceptive use between 1995 and 2005, a trend that was particularly prevalent among low-income countries [15]. DMPA scale up has been described in several countries including Bangladesh [16], Uganda [17], Ghana [15], Vietnam [18, 19], Taiwan [20], Afghanistan [21], Malawi [22], India [23] and Zimbabwe (Rhodesia) [24]. As a well-
documented reproductive health technology that has scaled up in diverse contexts, DMPA offers an exemplar “product-type” innovation in the domain of family health for illustrating the AIDED model’s usefulness. We selected DMPA rather than other injectable contraceptives on account of its longer duration, which is a distinguishing feature that is advantageous in settings where access to health care is difficult; DMPA is also the most prevalent injectable contraceptive used globally [15, 25].

Previous literature about scaling up DMPA has tended to focus on the distribution channel, such as whether clinic-based or community-based distribution is used. Numerous findings related to the safety and efficacy of community-based distribution (CBD) of DMPA have been published [10-12, 14, 23, 26-29] and recently synthesized [11] and toolkits to aid policy makers and practitioners in scaling up community-based access to injectables have also been produced [30-33]. By contrast, this paper seeks to synthesize evidence about the enabling factors and barriers to scale up of DMPA as a product, rather than scale up of a particular DMPA distribution channel. Our focus is therefore on cases in which DMPA use has spread from a smaller number to a larger number of user groups, regardless of whether that spread occurred via clinic-based or community-based approaches. In this paper we map the evidence about DMPA scale up to the AIDED model, summarizing relevant peer-reviewed and grey literature to illustrate the model with a specific product innovation, and identify lessons for scaling up of DMPA and other contraceptive technologies in low- and middle-income countries.

The AIDED Model (Pp. 4-6): The AIDED model includes 5 non-linear, interrelated components: 1) assess the landscape, 2) innovate to fit user receptivity, 3) develop support, 4) engage user groups, and 5) devolve efforts for spreading innovation [9]. Each component captures a set of processes; this action-based approach distinguishes the AIDED model from other scale up frameworks that focus on actors or context [2-4, 6, 34]. The model suggests that successful scale up occurs within a complex adaptive system, characterized by interdependent parts, multiple feedback loops, and several potential paths to achieve intended outcomes. The AIDED model’s nonlinear nature is another distinctive feature relative to existing approaches to scale up strategy design [1, 35]. Importantly, the AIDED model was developed with groups (e.g., organization or community) as its unit of analysis and mechanism of spread, in contrast to prior scale-up studies of individual behavior change [36-38].

The ASSESS component refers to assessment of the broad landscape within a potential user group, including the needs and wants of the user community, its absorptive capacity, and the political, economic, legal/regulatory, technological and social conditions within its internal and external environment. The INNOVATE component includes designing, re-designing, and packaging an innovation so that the innovation is acceptable and perceived as advantageous by potential user groups in their specific context or environment. These processes of designing, re-designing, and packaging the innovation are aimed at achieving ‘fit’ between the innovation and the user group. In the DEVELOP component, attention is directed to fostering enabling relationships, environments and networks among partners that can support and facilitate spread of the innovation. Although engagement occurs throughout the process of dissemination and diffusion, the ENGAGE component involves the specific tasks of introducing the innovation from outside the user group to inside the user group, translating the innovation so that user groups can assimilate the new information, and integrating the innovation into the routine practices and social norms of the user group. Finally, the DEVOLVE component involves the initial user groups releasing and spreading the innovation for its re-introduction in new user groups within their peer networks. These user groups and their networks replicate and release the innovation (in adapted and potentially failed forms) in the way they see most appropriate.
The AIDED model is both descriptive of common features of successful innovation spread, and prescriptive of processes that should be considered by those wishing to facilitate scale up.

Comment #2
Why did the authors select scale-up of DMPA and how is scale-up defined by the authors? Did the scope or scale of the scale-up matter? Did it matter if the project focused on task shifting or if it was new introduction of the product?

Response
We have added language to the Background and Methods to explain our choice of DMPA and the definitions of scale up used in our literature review as follows:

**Background (P. 4):** As a well-documented reproductive health technology that has scaled up in diverse contexts, DMPA offers an exemplar “product-type” innovation in the domain of family health for illustrating the AIDED model’s usefulness. We selected DMPA rather than other injectable contraceptives on account of its longer duration, which is a distinguishing feature that is advantageous in settings where access to health care is difficult; DMPA is also the most prevalent injectable contraceptive used globally [15, 25].

**Methods (Pp. 6-7):** We used two questions to determine if an article fit our study objective of identifying factors associated with DMPA scale up:
(i) Does the paper specifically address factors related to an increase in the number of individual DMPA users within a given group or community?
(ii) Does the paper specifically address factors related to the diffusion, dissemination, or scale up of DMPA use from one geography to another (e.g., from village to village, or province to province)?

If the answer to either question (i) or question (ii) was affirmative, the paper was included in our sample. We did not set any minimum criteria for the scope or scale of scale up. We included cases in which DMPA was introduced to end user groups for whom DMPA was new, whether such expanded delivery occurred through task shifting (e.g., from clinic-based providers to community-based health workers) or a first-time introduction of DMPA into a country or health system.

Comment #3
Please explain what is meant by the 3 studies that did not meet the “definition of Depo-Provera” (page 5).

Response
Thank you for drawing our attention to the imprecision of this language. We have rephrased the references to the “definition of Depo-Provera” as follows (see underlined text):

**Methods (P. 7):** An article was excluded at the abstract screening stage if it did not address spread of DMPA as an injectable contraceptive as its primary topic (n=218) or if it did not discuss the scale up or sustainability of DMPA (n=37).

**Methods (P. 7):** At the full text screening stage, an article was excluded if: (1) it was superficial in its discussion and/or did not provide empirical evidence about the scale up or sustainability of DMPA(n=7); (2) it did not address scale up or sustainability of DMPA (n=4), did not address
spread of DMPA as an injectable contraceptive as its primary topic (n=3), did not address low- or middle-income countries (n=3); or (3) the full text of the article was not available online (n=1).

Figure 1 (in Abstract Review box): Does not address DMPA spread as its primary topic (n=218)

Figure 1 (in Full Text Review box): Does not address DMPA spread as its primary topic (n=3)

The majority of the articles excluded under this criterion were scientific articles about the biochemical properties and effects of DMPA, clinical trials of DMPA, or DMPA’s use in high-income settings.

Comment #4
The authors chose to include projects which focused on scale-up of community-based provision as well as clinic-based provision. If the authors choose to retain this focus the background section and abstract should be revised to reflect the larger view of DMPA provision.

Response
We recognize and agree that there is an important distinction between clinic-based and community-based services. We appreciate your suggestion and have revised the Abstract and Background sections accordingly to clarify that the focus of our study was on scale up of DMPA as a contraceptive product, rather than scale up of community-based distribution of DMPA as a delivery method:

Abstract (p. 2): Use of depot medroxyprogesterone acetate (DMPA), often known by the brand name Depo-Provera, has increased globally, particularly in multiple low- and middle-income countries (LMICs). As a reproductive health technology that has scaled up in diverse contexts, DMPA is an exemplar product innovation with which to illustrate the utility of the AIDED model for scaling up family health innovations.

Background (p. 4): Previous literature about scaling up DMPA has tended to focus on the distribution channel, such as whether clinic-based or community-based distribution is used. Numerous findings related to the safety and efficacy of community-based distribution (CBD) of DMPA have been published [10-12, 14, 23, 26-29] and recently synthesized [11] and toolkits to aid policy makers and practitioners in scaling up community-based access to injectables have also been produced [30-33]. By contrast, this paper seeks to synthesize evidence about the enabling factors and barriers to scale up of DMPA as a product, rather than scale up of a particular DMPA distribution channel. Our focus is therefore on cases in which DMPA use has spread from a smaller number to a larger number of user groups, regardless of whether that spread occurred via clinic-based or community-based approaches. In this paper we map the evidence about DMPA scale up to the AIDED model, summarizing relevant peer-reviewed and grey literature to illustrate the model with a specific product innovation, and identify lessons for scaling up of DMPA and other contraceptive technologies in low- and middle-income countries.

Comment #5
I would like to know more about the data extraction process. How did authors decide if a project had the characteristics of each component of not?

Response
Thank you for your interest in this process. We have added a paragraph to the Methods section to explain how enabling factors and barriers were mapped to the five AIDED model components:
Methods (P. 8): After the final list of enabling factors and barriers was established, two team members mapped these scale up determinants to the five components of the AIDED model (ASSESS, INNOVATE, DEVELOP, ENGAGE, and DEVOLVE). The mapping was conducted by comparing each enabling factor or barrier against the definitions of the five components to determine if it fit into one or more parts of the AIDED model. For example, the enabling factor of “ensuring fit with cultural norms” was mapped to both the ASSESS and INNOVATE components because ensuring fit with cultural norms requires identifying the extant norms (an aspect of assessment) and then tailoring the product to be acceptable within those norms (an aspect of innovation design and packaging). This process preserved the potential for an enabling factor or barrier not to match the definition of any of the five components. Disagreements between the two team members were resolved through negotiated consensus.

Discretionary Revisions

Comment #6
A great deal of effort was taken to describe the study design of each article used in the systematic review, but the study questions for these papers are unclear. The reader doesn’t have a sense of the scope, pace, or scale of the scale up. Also the paper seems to treat all projects as equal. Were some of the projects more or less successful? It would add credibility to your analysis if you found more of the AIDED characteristics in projects that scale-up faster, implemented at greater scale or were sustained over a longer period of time.

Response
Thank you for your comment. We have added language to the Methods to clarify that we did not set a minimum criteria for the scope or scale of scale up in selecting our literature sample:

Methods (P. 6): We did not set any minimum criteria for the scope or scale of scale up.

Our analysis therefore does treat all projects as equal, although we see this as a strength in demonstrating the applicability of the AIDED model to diverse cases. Nevertheless, we agree that analyzing the presence of the AIDED characteristics in terms of the scope, pace, and scale of the scale up would be very valuable. Unfortunately, many of the studies included in our sample did not provide adequate data on all aspects of the scale up process to enable us to conduct such an analysis. We also agree with the author about the need for future research and appreciate the specific suggestion. We have noted the scope issue as a limitation and an area for future research in the Discussion section:

Discussion (P. 19, edit underlined): First, many of the articles in our sample did not describe all stages of the scale up process in equivalent levels of detail. As a result, we were unable to disaggregate our analysis in terms of the scope, pace, or extent of scale up in the cases we examined.

Discussion (P. 20): An important area for future research would be to analyze the presence of the different AIDED model components according to the scope, pace, and extent of scale up to determine whether more AIDED characteristics were present in projects that were scaled up faster, implemented at greater scale, or sustained over a longer period of time.
Comment #7
I challenge the notion that scale up of clinic based innovations is the same as community based innovations. Clinical delivery is supported by the larger health system while community based provision functions as a quasi part of the system. I believe these are fundamentally differences and would like to see the analysis disaggregate by these types of scale-up to see if the authors’ assumption hold true.

Response
Thank you for your suggestion to disaggregate the analysis by the type of DMPA distribution system used. We agree that there are important differences between clinic-based and community-based distribution that merit further investigation in terms of the applicability of the AIDED model. Unfortunately, the literature that we reviewed did not consistently emphasize the type of distribution channel used. Moreover, as our aim in this paper was to illustrate the AIDED model using DMPA as a contraceptive product rather than a specific distribution system for DMPA, we have not disaggregated the analysis by type of distribution; however, we have added this as an area for future research in the Discussion section:

Discussion (P. 20): Another area for future research is the application of the AIDED model to the scale up of different distribution systems for DMPA, specifically clinic-based versus community-based, to determine if particular AIDED model components are differentially represented across these distribution approaches.
Reference list from revised manuscript

Note: new references added to the manuscript during revisions are indicated with **


2. ExpandNet. Scaling up health innovations. [http://www.expandnet.net/home.htm]


5. Subramanian S, Naimoli J, Matsubayashi T, Peters DH: Do we have the right models for scaling up health services to achieve the Millennium Development Goals? BMC Health Serv Res 2011, 11:336.


31.** FHI360, USAID. Community-based access to injectable contraceptives toolkit. 2013. [http://www.k4health.org/toolkits/cba2i]


