ARC SAC SCIENTIFIC REVIEW
Hemostatic Agents

Questions to be addressed:

Original Question (2009):

Is the use of hemostatic agents by the civilian layperson community and trained responders effective, appropriate and applicable in the out-of-hospital setting?

Updated Question (2015, 2019):

For patients with profuse/severe hemorrhage/bleeding from a traumatic skin wound being treated by community lay persons or trained responders (P), does the use of hemostatic agents in addition to standard first aid hemorrhage control measures of direct pressure with or without a bandage on the wound (I) compared to treatment with standard first aid hemorrhage control measures of direct pressure alone (C) decrease time to stopping bleeding, volume of blood loss, incidence of shock, incidence of complications or incidence of death.

Introduction/Overview:

This literature review was first conducted 6-9-2009 in formulation of a position paper for the American Red Cross Advisory Council on First Aid, Aquatics, Safety and Preparedness (ACFASP) to evaluate the efficacy for use of hemostatic agents by the general public for external hemorrhage events. As a comparative analysis to current acceptable practices for control of bleeding (ARC Guidelines for First Aid, December 2005, Part 14) a literature review to determine the use of hemostatic agents by civilian layperson community and trained responders as effective, appropriate and applicable in the out-of-hospital setting was undertaken. Current literature indicates varying degrees of efficacy based on product utilized, type of bleeding and educational methodologies used for implementation by military and emergency medical service providers.

2019 Background/Introduction:

Hemostatic agents have become an important tool in the care of the severely bleeding patient by both the military and the civilian emergency medical response agencies. These products have been studied in laboratory settings and approved for use in humans for skin wounds for over two decades. The use of these products has gained continued attention over the past 20 years, since first being incorporated in the US Military Tactical Combat Care plan. Hemostatic agents come in various forms. Currently, hemostatic impregnated gauze is the most common form, although injectable mini-sponges are designed for cavitary lesions. Other agents in development for the future may include foam or spray applicators. Granular or power forms of hemostatic agents were initially used when these agents were first developed but have fallen out of favor with the development of more user-friendly forms of agents. This review includes agents that are currently available for use, whether over the counter or by prescription.

Hemostatic agent use has been reviewed and guidelines developed by a several organizations in the most recent 8 years. Two of those evidence reviews, including one focused on pre-hospital emergency medical providers, and the other focused on first aid providers, were closely aligned with the 2015 ARCSAC PICOST, as described below. For the 2019 ARCSAC review, these similar reviews were utilized as a foundation for evaluating the additional evidence in the interim since the last Triennial Review.

Background

The use of agents for control of bleeding is documented as early as ancient Egyptian culture.[1] The initial First Aid course by the Red Cross was initiated prior to the first World War.[2] In 1966 the National Academy of Sciences identified deficiencies in providing emergency medical care in the United States and released a "White Paper" entitled Accidental Death and Disability: The Neglected Disease of Modern Society [3]. The foundation for the White Paper originated from comparisons of statistics which identified more civilians died on the roadways of the United States from traumatic injury than soldiers being injured in the Korean War. Methodologies for treating the wounded during the Korean War took tremendous strides forward with the increased utilization of Mobile Army Surgical Hospitals and rapid evacuation of the injured to these facilities. The provision of basic education for first aid to the general lay public and public services (Fire, Police and Ambulance) has occurred through various forms of educational programs, most notably the American Red Cross First Aid Training Program.

Hemostatic Agents

With the advent of hemostatic products now being made available to consumers, lay persons and EMS personnel alike, an evidenced based literature review was conducted to evaluate the efficacy and applicability of these agents in the out-of-hospital environment.

The use of hemostatic agents is able to be dated back to ancient Egyptian time periods where fresh meat was utilized as an "efficient hemostatic and mechanical agent." [1] More recent products have been developed with varying efficacy, with the foundation for utilization outside of the hospital environment predominantly derived from animal studies and case reports. Hemorrhage control has been a priority for the Department of Defense Combat Care Research Program for the last 10 years [4] with active development and evaluation of alternative pressure type pressure dressings such as BioHemostat [5], chitosan and fibrin hemostatic agents. With hemostatic agents, various compounds are utilized to facilitate coagulation at the site of the injury. The effectiveness of these agents is measured in time to hemostasis based on the type and severity of the injury. The two primary agents being investigated either add a substance to a wound which increase the concentration of local clotting factors with chitosan, a naturally occurring, biocompatible polysaccharide derived from shrimp shells, or by increasing the availability of clotting factors with fibrin. [5] Both types of agents serve to facilitate the formation of a clot at the site of the injury through direct application. Currently, the utilization of

hemostatic agents has been predominantly limited to researchers and the military under laboratory and combatant situations. [4,6,7]. Agents such as the BioHemostat® pressure dressing are inserted directly into a wound and rapidly absorbs blood, creating a tamponade effect with back pressure applied to the damaged vessels.

The study of hemotstatic agents and their applicability in the out-of-hospital setting has primarily focused on use during military operations and limited implementation within the civilian emergency medical system. A retrospective analysis of a 21% failure rate by emergency medical providers identifies the need to define appropriate injury severity application and initial and continuing educational methodologies.[8]

Search Strategy and Literature Search Performed

2012 Updated Review Process and Literature Search Performed:

In an evaluation of "hemostatic agents" the following results were elicited:

Search.cochrane.org and MEDLINE databases elicited no articles related to use of hemostatic agents in the out-of-hospital environment. PubMed.org indicated less than five articles where hemostatic agents were evaluated in the out-of-hospital environment, primarily related to a retrospective analysis of anecdotal reports received from military personnel in combat situations. Key literature reviewed listed below.

2015 Updated Review Process and Literature Search Performed:

1. Search string development

Patient population
Adults and children
Out of hospital
Prehospital
First aid setting
Intervention
Hemostatic agent* (* allows PubMed to search for all possible endings: s, ing, ed)
Comparison
Bandages
Dressings
Gauze
First Aid
(Pressure was not searched individually due to being a term with such broad interpretation)
Outcomes
Hemorrhage volume
Hemostasis

Shock
Death

2. Search Strings Used by Other Recent Literature Reviews

Search String used by ECRI Institute for PubMed search(via OVID interface)

((("pre hospital" OR "pre-hospital" OR "prehospital" OR "emergency medical services" OR triage OR EMT OR "emergency medical technician" OR "emergency medical technicians" OR "emergency responder" OR "emergency responders" OR "first responder" OR "first responders" OR police* OR firefight* OR medic OR medics OR trauma OR life support OR rescue OR accident* OR ambulance* OR ((car OR vehicle) AND crash*) OR combat OR disaster* OR casualt* OR Veteran* OR military OR soldier* OR armed forces OR navy OR naval OR air force OR marines OR army OR combat OR war OR battle* OR "Iraq war" OR "Iraqi freedom" OR ((afghan OR Afghanistan) AND war))) AND (wound* OR injury OR injuries OR injured OR hemorrhage* OR haemorrhag* OR bleeding OR exsanguinate*)) AND (((Tourniquet* OR "combat application tourniquet" OR "combat application tourniquets")) OR ((((bandag* OR dressing* OR gauze* OR tape OR tapes OR taping OR sponge OR sponges) AND (hemostas* OR hemostat* OR coagulat* OR clot OR clotting OR clots OR fibrinolysis OR (fibrin AND (seal OR adhesive OR sealant)) OR stasis OR chitosan))) OR ("Combat Gauze" OR HemCon OR QuikCLot OR TraumaDEX OR BioHemostat OR CELOXTM OR modified rapid deployment hemostat OR "MRDH")))

Search string used by ILCOR

ILCOR background information, equivalent to raw data in a scientific study, is considered proprietary by the ILCOR, thus it cannot be reproduced here.
The PubMed search string developed by ILCOR was reviewed and, though different, not in major aspects from that developed by ECRI.

2. **Search String Modifications and Refinements**

Modifications

Since the ECRI search string was heavily weighted to military, combat and professional providers, a comparison search string was developed without these terms. A test search without these search terms led to a marked limitation in results. Although many of the issues of concern in first aid use of an intervention have to do with whether the intervention is simple enough and low risk enough that it would be considered effective and safe to be applied by minimally trained lay persons, based on a value assessment that stopping or significantly decreasing severe, potentially life-threatening bleeding is of high value, it seemed reasonable to seek as much information as possible in terms of the potential utility of the intervention. Thus, it was decided to perform the search for this review with the military, combat and professional-oriented search terms preserved.

The ECRI search process combined searching for information on tourniquets and hemostatic agents. For the purposes of these ARCSAC reviews, the search strings for each concept were used separately.

4. Final ARCSAC Search String for Hemostatic Agents

((((("pre hospital" OR "pre-hospital" OR "prehospital" OR "emergency medical services" OR triage OR EMT OR "emergency medical technician" OR "emergency medical technicians" OR "emergency responder" OR "emergency responders" OR "first responder" OR "first responders"

OR police* OR firefight* OR medic OR medics OR trauma OR life support OR rescue OR accident* OR ambulance* OR ((car OR vehicle) AND crash*) OR combat OR disaster* OR casualt* OR Veteran* OR military OR soldier* OR armed forces OR navy OR naval OR air force OR marines OR army OR combat OR war OR battle* OR "Iraq war" OR "Iraqi freedom" OR ((afghan OR Afghanistan) AND war)))) OR ((wound* OR injury OR injuries OR injured OR hemorrhage* OR haemorrhag* OR bleeding OR exsanguinate*))) AND (((((bandag* OR dressing* OR gauze* OR tape OR tapes OR taping OR sponge OR sponges) AND (hemostas* OR hemostat* OR coagulat* OR clot OR clotting OR clots OR (fibrin AND (seal OR adhesive OR sealant)) OR stasis OR chitosan)))) OR (("Combat Gauze" OR HemCon OR QuikCLot OR TraumaDEX OR BioHemostat OR CELOXTM OR modified rapid deployment hemostat OR "MRDH"))[all])

5. Search Limitatons

Date: Two date limit ranges were applied: an initial search limit from the date of the ECRI search, 03/18/2013 to date of final search, 06/10/2015 and a search from 5/30/2012, a date chosen shortly prior to the presentation of the last Triennial Review in June 2012, to the date of the ECRI search of 3/18/2013. The final working search was based on a date range from 05/30/2012 to 06/12/2015, the last date a search was performed prior to this current Triennial Review.

Language: English

6. Databases Searched

PubMed search of Medline database. ECRI Institute searched Medline and Embase via an OVID interface. Other databases searched by ECRI for the NHTSA review were not searched due to noting that all articles used by ECRI were in Medline search results.

7. Search Results

Search results titles were scanned to eliminate articles referring to surgical settings, wound healing and to collect articles referring to out of hospital management of traumatic wounds ideally in human clinical or in experimental animal settings as well as ones reporting observational case series. Case reports were not collected.

Attempts were made through electronic subscription access or reaching out to corresponding authors to obtain copies of articles for citations collected on screening of titles.

Ultimately articles were assessed for any influence they would have on modifying the current ARCSAC

The results of this screening process are presented in the following table.

Search Date Range	Citation Results	Title Review Results	Result of Abstract & Article Review for Articles with Impact on Recommendations
5/30/2012 - 3/18/2013	202		
3/18/2013 – 6/10/2015	391		
5/30/2012 – 6/10/2015	540	23	0(2)*

* Bulger et al. as representing the American College of Surgeons Committee on Trauma used the NHTSA funded Evidence Assessment report as a foundation for creating guidelines for prehospital external hemorrhage control (see above).

Of note, an initial screen of results was undertaken with exclusion of review articles, seeking only articles of experimental design. Thus, initial reporting of results was for 18 articles as there are 5 that would qualify as reviews.

Additionally, although the article by Hatamabadi reports on a randomized use of a hemostatic agent versus plain gauze on human clinical bleeding wounds, since both the wounds and the treatment prior to the ED assessment and treatment was not controlled, it is difficult to draw strong conclusions regarding the efficacy of the treatment.

8. Kept Article Summaries

Of the articles retrieved and summarized below, only one focused on human clinical care. Other articles addressed issues of efficacy of certain products under different conditions in animal models, often with application protocols that do not simulate clinical practice. For example, one study in a swine model of transection of the femoral artery tested the materials by first compressing the artery proximally, followed by sponging out the wound of any remaining free blood and then applying a layer of Vaseline gauze followed by the impregnated gauze test bandage material.

2019 Literature Search and Review Process:

After careful review of the legacy 2015 PICO and search strings, we believed them to be both compressive and appropriate. As such, the search strings were preserved for this 2019 TR. We sought to evaluate new contributions to the refereed literature since 2015 and to evaluate the impact of these additions

1. Search string

Patient population

Adults and children
Out of hospital
Prehospital
First aid setting

Intervention

Hemostatic agent* (* allows PubMed to search for all possible endings: s, ing, ed)

Comparison

Bandages
Dressings
Gauze
First Aid
(Pressure was not searched individually due to being a term with such broad interpretation)

Outcomes

Hemorrhage volume
Hemostasis
Shock
Death

2. Search Strings Used by Other Recent Literature Reviews

Search String used by ECRI Institute for PubMed search(via OVID interface)

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The 2015 TR authors did note that the PubMed search string developed by ILCOR was reviewed and, though different, not in major aspects from that developed by ECRI.

3. Search String Modifications and Refinements

Modifications

The previous 2015 TR search strings also separated for tourniquets and hemostatic agents.

4. Final 2019 ARCSAC Search String for Hemostatic Agents

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5. Search Limitations

Date: The final working search was based on a date range from 06/01/2015 through 02/12/2019.
Language: English

6. Databases Searched

PubMed search was performed by the ARC research librarian of Medline database.

7. Search Inclusion/Exclusion Criteria

Search results titles were scanned to eliminate articles referring to surgical settings, wound healing and to collect articles referring to out of hospital management of traumatic wounds ideally in human clinical or in experimental animal settings as well as ones reporting observational case series. Case reports were not collected.

Ultimately 7 articles were assessed for any influence they would have on modifying the current ARCSAC Scientific Review.

8. Search Results

The results of this screening process are presented in the following tables.

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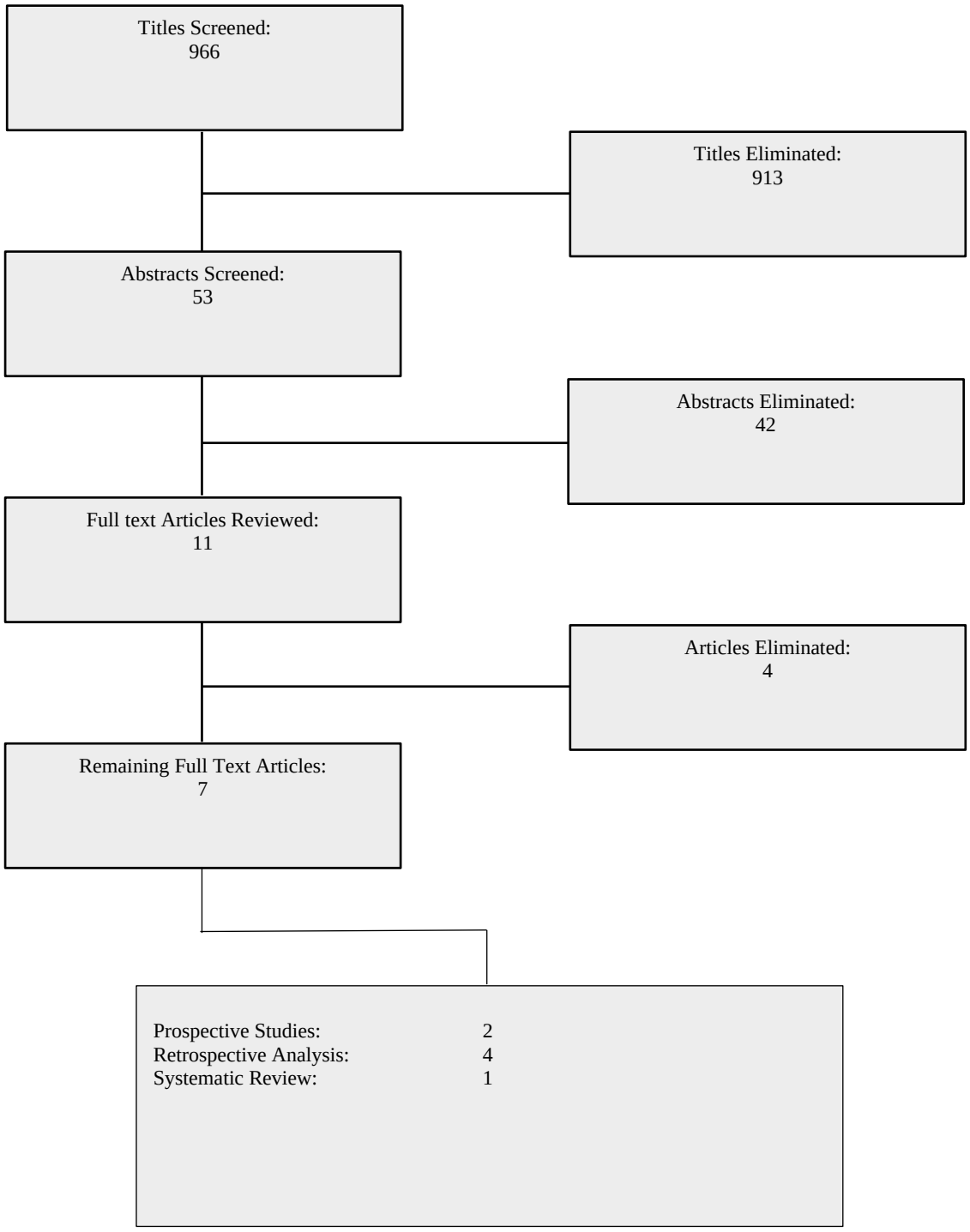
3/18/2013 – 6/10/2015	391		
5/30/2012 – 6/10/2015	540	23	0(2)*
6/10/2015 – 2/11/2019	966	11	7

2019 Hemostatic TR Screening Flow Diagram



9. Kept Article Summaries

Of the articles retrieved and summarized below:

- The majority of clinical evidence was retrospective.

- One randomized trial (Goolsby) demonstrated that lay persons can effectively apply gauze and were most successful with an injectable mini sponge delivery system.
- All studies that evaluated effectiveness of hemostatic gauze showed it to be effective in stopping or slowing bleeding.
- No studies concluded that hemostatic gauze was not effective.
- One study showed a survival benefit.
- Studies that used hemostatic gauze in clinical practice commonly used it as a second line intervention for when direct pressure was not effective.
- Retrospective studies also reported a large number of hemostatic gauze uses to effectively control bleeding on the head/scalp/face in addition to other body areas.

Scientific Foundation:
2012 Scientific Foundation:

Clotting

The body's physiologic response to blood loss from trauma, platelet abnormalities or deficiencies in coagulation factors, or from vascular defects includes a three phase process to facilitate the cessation of hemorrhage. In the initial phase, the muscular wall of a blood vessel contract to reduce the amount of blood flow and creates a turbulent flow of blood. This turbulent flow initiates the second phase of response by attracting platelets which adhere in the presence of collagen to the lining of the vessel, surrounding tissue and each other, further reducing blood flow through the vessel. While the initial clot that is formed in smaller vessels such as capillaries, small veins and arteries greatly decreases the loss of blood, it is extremely unstable. The third phase of coagulation strengthens the clot through the incorporation of fibrin and red blood cells, resulting in the expansion and strengthening of the clot.

Control of Bleeding

Failure to manage blood loss may result in an individual becoming hemodynamically compromised. This condition, known as shock, is defined as inadequate tissue perfusion. The inability of the body to perfuse oxygen to the cellular tissues and remove waste products may occur with as little as 15 to 20% loss of the total blood volume in adults. [9]

An overview of currently acceptable basic methods of hemorrhage control through direct pressure, defined as the application of pressure to the actual site of bleeding are reviewed below in order of progression based on injury severity, defined as:

1. Direct Pressure – To limit the loss of blood, placement of direct pressure over the injury site serves to compress vascular structures and promote localized clotting. Recommendations include sterile gauze in addition to a gloved hand.

2. Extremity Elevation – (Brown, DM, Worley, J. 2007) With concurrent use of direct pressure, the elevation of an involved extremity above the level of the heart to decrease

blood pressure through use of gravity will slow hemorrhage and promote localized clotting.

3. Direct Fingertip Pressure –Utilizes fingertips which are inserted into the wound with direct pressure for occlusion of the vascular hemorrhage.

4. Pressure Dressing – In the absence of controlled bleeding from direct pressure and extremity elevation, a dressing applied directly over the injury site under mechanical created by a firmly wrapped bandage. Distal pulses should remain intact unless severe arterial bleeding is present. Increase mechanical pressure as needed to control bleeding.

An additional method for the control of bleeding which occurs with or following use of hemostatic dressings is the application of a tourniquet. The application of a tourniquet and has been considered the last resort in cases where severe hemorrhage is life-threatening and not controlled through direct pressure and the use of hemostatic agents. The tourniquet is a constricting band placed between the heart and wound on an extremity, with the purpose of stopping all blood flow distal to the application point. Current literature identifies the absence of perfusion will promote anaerobic metabolites such as lactic acid and potassium to accumulate distal the application point, potentially causing systemic complications following the removal of tourniquet. [9]

Direct pressure, while widely accepted as a standard of practice for the control of all levels of injury severity, has limited discourse in the literature as to scientific research performed quantifying the applicability and efficacy of this instrument. A few studies comparing hemostatic agents reference the application of direct pressure, in context of a control for the experimental design of the studies.

The application of pressure directly on low pressure, size-limiting traumatic injuries to capillaries and veins is often effective in the presence of naturally occurring intrinsic and extrinsic clotting factors. A continuation of arterial blood flow distal the injury site decreases the effects of cellular anaerobic metabolites entering the central circulatory system in large quantities. The verification of hemostasis is readily accomplished through visual inspection.

Comparative Analysis

In reviewing the instruments utilized for control of bleeding in the out-of-hospital setting, the following evaluation based on applicability, vessel size, injury severity, effectiveness and other attributes (distal blood flow, thrombosis) were utilized to compare direct pressure with and without use of hemostatic agents.

Summary (2015)

Is the use of hemostatic agents by the civilian layperson community and/or trained responder effective, appropriate and applicable in the out-of-hospital setting?

This 2015 scientific review indicates hemostatic agents have **efficacy** in controlling hemorrhage which is unable to be controlled with direct pressure alone (Jackson, MR, Friedman, SA, Carter, AJ, Vladislav, BS, 1997; Larson, MJ, Bowersox, JC, Lim, RC, Hess, JR, 1995.) Implementation by military and civilian EMS trained responders demonstrated varying effectiveness secondary to appropriate utilization of the hemostatic agent instrument (Brown, DM, Worley, J, 2007; Wedmore, I, McManus, JG, Pusateri, AE, Holcomb, JE, 2006.) Currently, little discourse and no studies were identified for civilian laypersons utilizing hemostatic agents.

Based on the reviewed literature, the use of topical hemostatic agents by civilian laypersons is not currently supported. Studies are limited and isolated to out-of-hospital military and health care providers, with the **effectiveness** based on appropriate utilization (sized to injury, application directly to source of bleeding) for control of hemorrhage. As such, the **efficiency** cannot be determined without development and implementation of education methodologies with the ability for measuring practical application by the civilian community as well as identifying when victims need to follow-up with a trained healthcare provider.

Updated Scientific Foundation, 2015:

There is no real "new" scientific evidence to present in relation to the ARCSAC recommendations. The 2009 ARCSAC recommendations were based on what were classed as level 2a, 2c and 3 observational or non-randomized case series or animal models. The nature of the literature has not changed. Although there has now been a randomized study of what are termed 3rd generation hemostatic agents, ones based on Chitosan gauze, in civilian Emergency Department care[i], randomized double-blinded human studies do not exist even in animals. Thus, the level of evidence remains similar.

No studies were found to directly assess the use of hemostatic agents by lay or minimally trained first aid providers.

Recommendations from NHTSA and ILCOR Literature Reviews

NTHSA

- Information on the effectiveness of hemostatic dressings is centered on their ability to stop bleeding but little other outcome data related to human use have been reported in the available literature.

The NHTSA review was used by the American College of Trauma Committee on Trauma to formulate a guideline for prehospital medical personnel[ii]:

- We suggest the use of topical hemostatic agents, in combination with direct pressure, for the control of significant hemorrhage in the prehospital setting in anatomic areas where tourniquets cannot be applied and where sustained direct pressure alone is ineffective or impractical (Low Quality Evidence)
- We suggest that topical hemostatic agents be delivered in a gauze format that supports wound packing (Low Quality Evidence)

ILCOR

The ILCOR Consensus on Science and Treatment Recommendations draft document concludes

- We suggest (weak) hemostatic dressings* be used when standard first aid hemorrhage control cannot control bleeding by first aid providers; very low quality of evidence.

2015 Discussion Regarding Update of Recommendations

The 2012 Triennial Review recommendation was a reaffirmation of the 2009 initial guidance which affirmed that "the use of topical hemostatic agents has efficacy in controlling life-threatening bleeding when used in conjunction with Direct Pressure or Tourniquet." It continues to qualify this as being "when applied by trained personnel." The document states that "there remains no evidence to support the use of topical hemostatic agents by lay community responders" and that "there is no evidence for use of topical hemostatic agents for non-life threatening bleeding." Additionally, it is noted that "there is no evidence to make topical hemostatic agents available in first aid kits for the lay/non-trained public."

Prior to the beginning of the wars in Iraq and Afghanistan, the use of materials to assist with hemostasis other than simple gauze for packing was largely limited to the use of forms of gelatin in surgical procedures. In response to the rapidly increasing numbers of combat casualties with external hemorrhage from explosions and the high mortality from exsanguination, the US military aggressively pursued solutions and continued refinements. As of the time of this writing in mid 2016, hemostatic agents used by the US military are referred to as 3rd generation. And more are being presented in the scientific literature from laboratories around the world.

As these products have progressed from powders that interacted with blood and produced an exothermic reaction to the point of damaging tissues to chitosan, a linear polysaccharide produced from crustacean shells which functions by cross-linking with red blood cells to promote clotting.

In the US and British military, hemostatic bandages are now widely distributed soldiers entering combat. Small studies have demonstrated that, although the results are better when trained persons use them, untrained persons are able to employ them to establish initial hemostasis without any instructions.[iii] At the same time, despite numerous studies of the relatively improved hemostasis and decreased blood loss with the various agents, success is still dependent on packing and applying pressure. At least one study has found no advantage to either QuickClot™ or Celox Gauze ™, a rolled fabric made with nonwoven chitosan-derived fibers, over standard gauze with an experimental design that group felt to be more aligned with field practice.[iv] The standard swine femoral artery injury and treatment model involves drying out the wound, applying a Vaseline gauze in the depth of the wound followed by a layer of the test gauze, followed by rolled plain gauze to use as packing and onto which an operator applies 25 pounds of manual pressure for 5 minutes and is followed by an additional 30 minutes of 10 pounds of passive pressure. Watters used a model of applying the hemostatic agent or standard gauze directly into the blood filled wound with on-going active bleeding and then applying manual pressure for either the time recommended by the manufacturer or for 0 or 30 seconds, a time thought to be more representative of the needs of an injured soldier at risk from on-going fighting.

This review has made no attempt to assess the relative efficacy of different hemostatic agents. This is an evolving domain and products will come forth that would likely render assessment at any one time moot in a relatively short time.

Another aspect of the assessment of the place for hemostatic agents in the practice of first aid for severe hemorrhage is the increasing marketing by the various manufacturers and availability of these products to the general public along with online videos explaining how to use them. Thus, despite the potential for unnecessary cost, these materials are likely to be increasingly present in settings where people are at risk of suffering bleeding wounds. Thus, it does not seem appropriate to make a recommendation that they only be used by persons with training. At the same time, it does seem appropriate to recommend that all persons have training in first aid techniques that will provide a better understanding of how to most effectively use these adjuncts to the underlying principle of applying pressure to bleeding wounds.

2019 Updated Scientific Foundation

The studies added to the 2019 TR included gauze-based delivery systems for hemostatic agents. One study (Goolsby, et al) looked specifically at the population of minimally trained/lay responders and demonstrated their ability to use gauze folded in a manner similar to hemostatic gauze was as effective as regular gauze. This study did conclude that this population was most successful using an injectable mini-sponge material as opposed to a material that required manual packing into a cavitary wound. The other studies included in the 2019 TR yielded a demonstrated an increase in the body of scientific literature to support the efficacy, safety and benefit of hemostatic agents.

The 2015 Triennial Review recommendation was a reaffirmation of the 2012 TR, which was based on the initial guidance that affirmed “the use of topical hemostatic agents has efficacy in controlling life-threatening bleeding when used in conjunction with direct pressure or tourniquet.” This recommendation had included the qualifier: “when applied by trained personnel.”

While there has previously been no evidence to support the use of topical hemostatic agents by lay community responders, one study from the 2019 TR showed the ability of minimally trained laypersons use material folded similarly to hemostatic gauze to the same degree of as regular gauze. The 2019 TR also included several studies that demonstrated the effectiveness and minimal side effect profile of hemostatic gauze. There remains no evidence for use of topical hemostatic agents for non-life-threatening bleeding.

Since the 2015 TR, the use of hemostatic agents, mostly in the form of dressings, has continued to grow. Hemostatic dressings are now standard issue for military forces worldwide. In addition, this equipment can be found on an increasing number of emergency medical services ambulances and medevac helicopters. Lastly, through the direct messaging of bystander engagement campaigns such as Stop the Bleed, hemostatic dressings are increasingly found in locations such as airports, shopping malls, schools and public buildings.

Although this review did not intend to assess the relative efficacy of different hemostatic agents, several studies compared different hemostatic gauze product with varying conclusions. This remains an evolving domain with new products still in development.

Regarding the roll of hemostatic agents for use in first aid for severe hemorrhage, it is likely that hemostatic dressings will be increasingly present in settings where people are at risk of suffering bleeding wounds. The previous TR recommended their use only by persons with training, and that it seemed “appropriate to recommend that all training in first aid bleeding control techniques

address the role of these materials as adjuncts to the primary treatment of direct pressure for bleeding wounds".

In summary, there is a well-established body of evidence to demonstrate the effectiveness of hemostatic gauze. It remains difficult, due to data quality, to determine superiority of an individual hemostatic gauze product. Quick Clot Combat Gauze appears to be the most frequently encountered hemostatic gauze. Newer, injectable self-expanding mini sponge products show great promise for both ease of use and functional ability to stop bleeding. It is our overall assessment that hemostatic dressings appear to be effective in the control of bleeding, when compared to regular gauze and in situations not amenable to tourniquet use. Additionally, we did not find evidence that suggests plain gauze should be taught preferentially to First Aid practitioners instead of hemostatic dressing use. It is important to note that the scope of this triennial review did not include public health considerations, such as material cost, shelf life, etc. that would have an important impact on any eventual First Aid training recommendations.

Upon conclusion of this 2019 TR, we believe that there is a growing body of evidence to support the use and safety of hemostatic dressings. Previous recommendations supported the use of hemostatic gauze use when conventional direct pressure was not effective. Based upon this review, we believe it is appropriate to move from option to guideline regarding the use of hemostatic dressings.

Recommendations and Strength:

2009 and 2012 Recommendations and Strength (using table below):

Standards: None

Guidelines: None

Options:

Lay Community Responder: No evidence to support use of topical hemostatic agents

Trained Rescuer: With appropriate training, topical hemostatic agents are applicable in situations where initial direct pressure has failed to control hemorrhage. (Level II)

2015 Updated Recommendations:

Standards: None

Guidelines: None

Options: In cases of external hemorrhage not controlled by or not compatible for treatment with standard first aid including tourniquet, use of hemostatic agents can assist with decreasing hemorrhage.

2019 Updated Recommendations:

Standards: None

Guidelines: We suggest the use of a hemostatic dressings in cases of life-threatening external hemorrhage not amenable to treatment by tourniquet.

Options: None

Knowledge Gaps and Future Research:
None

Implications for ARC Programs:

The change from an option to a guideline for use of hemostatic agents should be communicated promptly to instructors via Instructors Corner and incorporated into the next edition of the First Aid Participants Manual.

Summary of Key Articles/Literature Found and Level of Evidence/Bibliography:

Author(s)	Full Citation	Summary of Article	Level of Evidence (Using table below)
Brown, DM, Worley, J	Experience with chitosan dressings in a civilian ems system, 2007, Journal of Emergency Medicine, In Press, Corrected Proof, Available online 19 November, 2007	The authors felt the use of this instrument was beneficial in the civilian environment. Self-reporting of data by personnel without independent validation of data, non-standardized times for and of direct pressure application, time to cessation of bleeding and lack of hospital follow-up are major limitations to this study. Educational process for providers addressing the 21% failure rate of utilization. Study indicated use of instrument may be more effective with penetrating injuries as seen more frequently in combat situations. Criteria: All EMS providers received training for product use via multimedia presentation without live tissue or hands-on product exposure. Initial intervention with standard direct pressure and elevation of injured area when possible. Saturation of gauze dressing with above criteria initiated warranted application of interventional tool (HemCon® dressing.) For suspected arterial bleeding the provider was permitted to proceed directly to the use of interventional tool. Time to application was left to the discretion of the provider. Removal instructions were provided to all receiving facilities. Applicability: Study implemented use on all injuries where bleeding was not controlled with direct pressure and elevation. 37 uses were recorded with three uses eliminated	2a Prospective analysis of utilization by emergency medical service personnel on the efficacy of hemostatic agents being utilized in the civilian prehospital setting.

		due to incomplete data. Use in 34 cases revealed no adverse events or complications. 53% involved extremities, 38% were head, neck and face. Wounds to the chest, abdomen and axilla comprised the remaining 9%. Vessel Size: 13 cases were reported as venous and 12 cases arterial. Nine cases were classified as unknown. Injury Severity: Seven cases reported cessation of bleeding did not occur within 10 minutes and two cases were between 5 and 10 minutes. Effectiveness: Hemorrhage was controlled within 3 minutes of application in 79% of cases. Instrument was successful in 76% of cases where direct pressure failed to control bleeding. In seven cases instrument failed to control bleeding within 10 minutes (21%). Six of the seven failure cases reported user error. Five cases reported coagulopathy present with effective control of bleeding by instrument.	
Wedmore, I, McManus, JG, Pusateri, AE, Holcomb, JE	A special report on the chitosan-based hemostatic dressing: experience in current combat operations. 2006, Lippincott Williams & Wilkins, Inc. March 60(3) : 655-58	Authors acknowledge study design was retrospective analysis of oral and limited written analysis of case studies based on active utilization of instrument increases possibility for recall bias. Additionally, no follow-up post application of the instrument was possible due to the environment and sensitive nature of ongoing war operations. In one failed case size of the bandage inhibited appropriate application. Modification was made by the shredding of the instrument with insertion into the wound with hemostasis being achieved. Criteria: Use of instrument with data collection days to weeks after usage due to remote locations and sensitivity / nature of missions.	2c A retrospective analysis of cases evaluating the efficacy of hemostatic bandages utilized by military personnel in active combat environment.

		Applicability: 55% utilization on extremities, 39% chest, groin, buttocks and abdomen; remaining 6% face and neck. No dressings were placed in the chest or abdominal cavity – external use only. Difficulty was experienced with small wounds without modification of size and shape to instrument. Vessel Size: 52% reported as venous, 11 % arterial and 37% unknown. Injury Severity: Review of these cases determined 45% uses benefited where a tourniquet could not be applied. Instrument was determined to have less utility in small extremity injuries. Over utilization was determined for 19% of the cases. Effectiveness: 66% of cases the instrument was utilized following traditional direct and pressure dressing interventions. Remaining 34% cases unknown if prior interventions were initiated. Bleeding was controlled or greatly reduced in 97% of the cases where visual application was achieved. 2% of the cases experienced failure, reportedly where large cavitational wounds existed and blind insertion of the instrument was performed.	
Jackson, MR, Friedman, SA, Carter, AJ, Vladislav, BS	Hemostatic efficacy of a fibrin sealant-based topical agent in a femoral artery injury model: a randomized, blinded, placebo-controlled study. 1997, Journal of	This study successfully demonstrated the efficacy of the instrument with large vessel, high pressure wounds. Utilized the measurement of direct pressure pressure as a constant for comparative analysis of control and instrument. Notable findings included the increase in blood flow under similar application of pressure that promoted continual distal blood flow and decreased risk of thrombosis. Authors suggest application of the instrument may benefit traumatically injured persons	3 Prospective study analyzing the effects of hemostatic agents versus control gauze on swine femoral arterial hemorrhage.

	Vascular Surgery, 26(2): 274-80	and use as an immediate intervention to hemorrhage on the battlefield. Criteria: Determine the efficacy of topical hemostatic agents with large vascular injury. Applicability: Authors sought to compare the instrument against a control (non-hemostatic agent dressing) through blinded, randomized, placebo-controlled study. Vessel Size: 4 mm surgical incisions were made in bilateral femoral arteries. Injury Severity: Methodology of study design evaluated large, high pressure vascular structure to simulate severe hemorrhage condition. Effectiveness: Significant reduction of blood loss was experienced by wounds with instrument application (4.9 vs 82.3 ml respectively) under consistent blood flow conditions. Cessation of bleeding was evaluated at 15 minutes with reporting of complete hemostasis for 83% of the instrument and 0% of the control wounds. With one failure due to incomplete contact with the wound, the instrument successfully controlled bleeding for 30 – 90 seconds during 75% of the 15 minute evaluation intervals. Other: Wounds treated with the instrument experienced an approximate 10% greater blood flow during the study.	
Larson, MJ, Bowersox, JC, Lim, RC, Hess, JR	Efficacy of a fibrin hemostatic bandage in controlling hemorrhage from	Authors believe intervention with instrument would be beneficial with a select population in the civilian where delayed transport to definitive care exists. This article was one of the earlier references about hemostatic	3 Prospective comparative analysis of hemostatic instrument and standard practice

	experimental arterial injuries. 1995, Archives of Surgery. 130(4): 420-22	agents and served as a foundation for development and implementation in the EMS industry. Criteria: Determine the efficacy of topical hemostatic agents with large vascular injury when compared to traditional pressure gauze dressings. Applicability: Authors sought to compare the instrument against a control (non-hemostatic agent dressing) through controlled study. Injury Severity: Methodology of study design evaluated large, high pressure vascular structure to simulate severe hemorrhage condition. Effectiveness: Following confirmation of free blood flow through the arteriotomy the control or instrument was placed in direct contact with the wound site. A 3.5 kg weight was applied to the site for 1 minute then removed. Continuous monitoring of arterial pressure distal the wound occurred during the experiment. Evaluation of blood loss was evaluated following a one hour time lapse from application. Analysis revealed the hemostatic instrument was approximately 6 times more effective with creating hemostasis and in maintaining arterial perfusion pressure. Other: Post arteriotomy and application of interventions the control group experienced a significant reduction in mean arterial pressure was experienced throughout the treatment period.	of direct pressure with gauze for control.
Walters, TJ, Wenke, JC, Dauvar, DS, McManus, JG, Holcomb, JB, Baer, DG	Effectiveness of Self-Applied Tourniquets in Human Volunteers, 2005,	Tourniquets which met the criteria and demonstrated ability to be effective in eliminating distal blood flow of extremities have potential to be implemented as	3 An assessment of multiple tourniquets for effectiveness by self-application

	Prehospital Emergency Care, 9:416-22	life-saving measures with severe extremity hemorrhage. Criteria: Required weight less than 230 grams; minimum strap width 1 inch; less than 1 minute to apply; easy release and reapplication; no external power requirements. Other desirable criteria included strap width not less than 2 inches; one-handed; self-application to upper extremity; capability of application to trapped limbs; protection from over-tightening; predicted cost not greater than $25 per unit Applicability: Seven of the original nine tourniquets evaluated were utilized with the study. Experiment I, three of the tourniquets were effective in eliminating distal blood flow in the leg of all subjects. Two were discontinued after multiple failures of the device. Experiment II evaluated four of the original nine devices where three experienced 100% effectiveness and one failure secondary to unbearable pain. Vessel Size: Three tourniquets in Experiment I demonstrated 100% success occlusion of circulation; of the remaining, one demonstrated 88%, one 67%, one 44% and one 22% effectiveness. Injury Severity and Effectiveness: Three of the seven tourniquets evaluated demonstrated effectiveness based on the criteria of 80% successful loss of distal Doppler auscultation without equipment failure.	as demonstrated by the elimination of Doppler signal by auscultation; Intolerable pain from tourniquet; Malfunction of tourniquet

2015 Summary of Key Articles/Literature Found and Level of Evidence/Bibliography:

	Author(s)	Full Citation	Summary Points and Commentary	Basis for not having major impact
01	Bennett, B. L., & Littlejohn, L	Bennett BL, Littlejohn L. Review of new topical hemostatic dressings for	Chitosan-based dressing material was judged to have apparent superiority to kaolin materials.	Review of earlier literature on several, then newer hemostatic agents.

		combat casualty care. Mil Med 2014;179:497-514.		
02	Bennett BL, Littlejohn LF, Kheirabadi BS, et al.	Bennett BL, Littlejohn LF, Kheirabadi BS, et al. Management of External Hemorrhage in Tactical Combat Casualty Care: Chitosan-Based Hemostatic Gauze Dressings - TCCC Guidelines-Change 13-05. J Spec Oper Med 2014;14:40-57	Authors review literature in support of a proposal to update TCCC Guidelines to include Chitosan-based hemostatic agents along with the then preferred agent, Combat Gauze.	Literature review and product descripbtions.
03	Bulger EM, Snyder D, Schoelles K, et al.	Bulger EM, Snyder D, Schoelles K, et al. An evidence-based prehospital guideline for external hemorrhage control: American College of Surgeons Committee on Trauma. Prehosp Emerg Care 2014;18:163-73.	Guidelines based on NHTSA evidence review	No major change from prior guidance. Underlying report search strategies used to develop this Triennial Review
04	Burnett LR, Richter JG, Rahmany MB, et al.	Burnett LR, Richter JG, Rahmany MB, et al. Novel keratin (KeraStat) and polyurethane (Nanosan(R)-Sorb) biomaterials are hemostatic in a porcine lethal extremity hemorrhage model. Journal of biomaterials applications. Feb 2014;28(6):869-879.	Industry-based presentation of new products – author employed by manufacturer.	Early evaluation of specific products not generally available at this time.
05	Causey, M. W., McVay, D. P., Miller, S., Beekley, A., & Martin, M.	Causey, M. W., McVay, D. P., Miller, S., Beekley, A., & Martin, M. (2012). The efficacy of Combat Gauze in extreme physiologic conditions. J Surg Res, 177(2), 301-305. doi: 10.1016/j.jss.2012.06.020	Kaolin impregnated rolled gauze (Combat Gauze – CG) was evaluated compared to non-impregnated rolled gauze (Standard Gauze – SG) in an acidotic and coagulopathic swine model of severe hemorrhage using transected femoral arteries. The bleeding was stopped by proximal direct pressure on the artery prior to placement of the test materials.	Although the CG was associated with faster clotting and less bleeding than the SG, this did not add significantly to or change prior understanding. The model was not the same as that used by Watters.(See discussion below.)[v]
06	Drew B, Bennett BL, Littlejohn L.	Drew B, Bennett BL, Littlejohn L. Application of Current Hemorrhage Control Techniques for Backcountry Care: Part One, Tourniquets and Hemorrhage Control Adjuncts. Wilderness Environ Med 2015;26:236-45.	Review article with guidance for hemorrhage control in wilderness and austere settings	Review article – did not add to knowledge base. Any references after beginning of search date were captured in search string application.
07	Garcia-Blanco J, Gegel B, Burgert J, Johnson S, Johnson D.	Garcia-Blanco J, Gegel B, Burgert J, Johnson S, Johnson D. The Effects of Movement on Hemorrhage When QuikClot(R) Combat Gauze Is Used in a Hypothermic Hemodiluted Porcine Model. J Spec Oper Med 2015;15:57-60.	Study reported evaluation of ability of clot formed in wounds treated with QCG vs "a control wound dressing" through putting hip joint (femoral artery injury) through motion. QCG-treated lesions had significantly less breakdown of clot than control-treated lesions.	No fundamental change in perspective that hemostatic agent is an adjunct to standard treatment.
08	Gegel B, Burgert J, Loughren M, Johnson D.	Gegel B, Burgert J, Loughren M, Johnson D. The effects of BleedArrest on hemorrhage control in a porcine model. US	Standard swine femoral artery lesion with 5 min manual and 30 min passive pressure. At one minute after stopping pressure and removing bulky dressings the	Evaluation of a specific agent – no change in basic principles

		Army Medical Department journal 2012:31-5.	amount of initial bleeding was not found to be statistically significantly (p=.533) different. The BleedArrest group ranged from 492 to 1569 mL (mean=789.22, SD±121.60 mL) and control group ranged from 100 to 992 mL (mean=601.50, SD±84.03 mL).	
09	Gegel BT, Austin PN, Johnson AD.	Gegel BT, Austin PN, Johnson AD. An evidence-based review of the use of a combat gauze (QuikClot) for hemorrhage control. AANA journal 2013;81:453-8.	Nursing journal evidence-based review with a PICO of "Is QuikClot Combat Gauze, a hemostatic agent, effective and safe in controlling hemorrhage in trauma patients in the prehospital setting?" "It did not conclusively demonstrate that this combat gauze is an effective hemostatic agent for use in trauma patients, but the results are promising in supporting its use."	Review limited to one product with "non conclusive" findings.
10	Grissom TE, Fang R.	Grissom TE, Fang R. Topical hemostatic agents and dressings in the prehospital setting. Current opinion in anaesthesiology 2015;28:210-6.	Abstract only available for review. Commentary that Chitosan agents appear equally efficacious to current dressings and a call for more study.	Opinion piece
11	Hatamabadi HR, Asayesh Zarchi F, Kariman H, Arhami Dolatabadi A, Tabatabaey A, Amini A.	Hatamabadi HR, Asayesh Zarchi F, Kariman H, Arhami Dolatabadi A, Tabatabaey A, Amini A. Celox-coated gauze for the treatment of civilian penetrating trauma: a randomized clinical trial. Trauma monthly 2015;20:e23862.	Evaluation of Celox (chitosan)-impregnated gauze compared randomly to untreated gauze dressings in a variety of civilian penetrating trauma wounds. Celox gauze-treated wounds overall bled less (treating physician count of "soaked" pads) and more wounds achieved hemostasis in first 5 min.	First civilian comparative trial of chitosan-gauze to untreated gauze. Consistent with animal studies of added hemostatic effect in civilian population. No fundamental change other than a new agent.
12	Hillis GR, Yi CJ, Amrani DL, et al.	Hillis GR, Yi CJ, Amrani DL, et al. Evaluation of NuStat?, a Novel Nonimpregnated Hemostatic Dressing, Compared With Combat Gauze in Severe Traumatic Porcine Hemorrhage Model. J Spec Oper Med. Winter 2014;14(4):41-47.	This article reported a study comparing a silica/cellulose dressing (NuStat = NS) to Combat Gauze (CG) in a swine femoral artery wound model. 3 min manual pressure with each agent. At release of pressure, NS was reported better for immediate hemostasis (p = .0475), duration of application time (p = .0093), use of resuscitative fluids (p = .0042) and additional blood loss after application (p = .0385). The two were reported equivalent at 60min	Study of novel product. No fundamental effect on concept of hemostatic utility.
13	Johnson D, Bates S, Nukalo S, et al.	Johnson D, Bates S, Nukalo S, et al. The effects of QuikClot Combat Gauze on hemorrhage control in the presence of hemodilution and hypothermia. Annals of medicine and surgery (2012). Jun 2014;3(2):21-25.	Swine were rendered hemodiluted and hypothermic following which a femoral artery/vein transection was performed. Following 1 min. free bleeding, pressure to stop, Vaseline gauze, QGC or Plain gauze packing with manual pressure for 5 min and 30 min	Experimental evaluation in a specific pathological situation of agent with proven capacity as hemostatic. No

			weight. QGC 11/13 & PG 4/13 w/ hemostasis. Significantly less failures with QGC and more resuscitation fluid needed prior to rebleed.	fundamental change in practice.
14	Johnson D, Westbrook DM, Phelps D, et al.	Johnson D, Westbrook DM, Phelps D, et al. The effects of QuikClot Combat Gauze on hemorrhage control when used in a porcine model of lethal femoral injury. Am J Disaster Med. Fall 2014;9(4):309-315.	Abstract only available to this reviewer. In a porcine femoral artery injury model, application of QuickClot Combat Gauze with standard packing vs standard packing, both with 5 min firm manual pressure followed by a "pressure dressing." Dressings removed after 30 min & blood loss calculated. If no bleeding, first phenylephrine, then volume then motion were introduced to provoke bleeding. QCG "was more effective in controlling hemorrhage, withstanding increases in systolic blood pressure, more latitude in resuscitation fluid, and movement ($p < 0.05$)."	Further evidence that kaolin dressings help promote hemostasis. No new information on fundamental principles.
15	Johnson D, Agee S, Reed A, et al.	Johnson D, Agee S, Reed A, et al. The effects of QuikClot Combat Gauze on hemorrhage control in the presence of hemodilution. US Army Medical Department journal 2012:36-9.	Swine model, femoral artery/vein transection, removed 30% blood volume loss then replenish with LR in 3:1 ratio. Then transected a/v, let bleed 60 sec. – packed petrolatum gauze then either QCG or standard gauze. 25 psi X 5min manually then 10lb wt X 30 min. Blood loss total and at different time points eval'd. Significant difference b/w groups.	Further analysis of hemostatic already known to be effective, simply in experimental model to represent another clinical situation. No major new or changing information.
16	Kragh JF, Jr., Steinbaugh J, Parsons DL, Mabry RL, Kheirabadi BS, Dubick MA	Kragh JF, Jr., Steinbaugh J, Parsons DL, Mabry RL, Kheirabadi BS, Dubick MA. A manikin model for study of wound-packing interventions to control out-of-hospital hemorrhage. Am J Emerg Med 2014;32:1130-1.	Letter to the editor with brief report of using a junctional wound tourniquet manikin for training wound packing technique with apparent success in 4 tests: packing, packing with overwrap, overwrap alone, packing with overwrap with air bladder inflated to apply pressure.	Evaluation of a training model for a technique not relevant to first aid.
17	Littlejohn L, Bennett BL, Drew B	Littlejohn L, Bennett BL, Drew B. Application of Current Hemorrhage Control Techniques for Backcountry Care: Part Two, Hemostatic Dressings and Other Adjuncts. Wilderness Environ Med 2015;26:246-54.	Discussion of types of hemostatic agents at the time of writing and brief review of some data to make recommendation of likely utility in heavily bleeding wounds that occur in austere civilian settings.	No new information.
18	Mortazavi S, Tavasoli A, Atefi M, et al.	Mortazavi S, Tavasoli A, Atefi M, et al. CoolClot, a novel hemostatic agent for controlling life-threatening arterial bleeding. World journal of emergency medicine 2013;4:123-7.	Dog femoral artery wounds were treated with a locally produced bentonite/zeolite mix either as powder or on gauze. With powder not much effect. With gauze at each of several time checks less bleeding was reported for the wounds treated with the novel mix.	This is an initial report of a novel product developed using materials either known to have hemostatic effect or from classes of materials know to have such effect. No

				information to change practice concepts.
19	Murray CK, Brunstetter T, Beckius M, Dunne JR, Mende K.	Murray CK, Brunstetter T, Beckius M, Dunne JR, Mende K. Evaluation of hemostatic field dressing for bacteria, mycobacteria, or fungus contamination. Mil Med 2013;178:e394-7.	Evaluation of stock samples of dressings for contamination. None was found	Addresses fundamental product safety. No impact on practice.
20	Rall JM, Cox JM, Songer AG, Cestero RF, Ross JD	Rall JM, Cox JM, Songer AG, Cestero RF, Ross JD. Comparison of novel hemostatic dressings with QuikClot combat gauze in a standardized swine model of uncontrolled hemorrhage. J Trauma Acute Care Surg. Aug 2013;75(2 Suppl 2):S150-156.	Evaluation of newer products to then-standard military issue QuickClot Gauze (QGC). Higher rates of survival, though not statistically significant were observed with newer, generally chitosan-based dressings compared to QGC	Comparisons of advances in product technology. Single study, though suggesting a practice update.
21	Satterly S, Nelson D, Zwintscher N, et al	Satterly S, Nelson D, Zwintscher N, et al. Hemostasis in a noncompressible hemorrhage model: an end-user evaluation of hemostatic agents in a proximal arterial injury. Journal of surgical education 2013;70:206-11.	Comparison of TC3-trained & CLS-trained soldiers in hemorrhage control – no difference at 2 min, TC3 20% better at 4 min. Combat Gauze rated easiest to use of 4 products by all participants. No significant difference in hemostasis among agents, though CG was associated with highest degree of hemostasis at 4 min.. (83%)	Comparison among products, though did demonstrated relative ease to use effectively with minimal training.
22	Smith AH, Laird C, Porter K, Bloch M.	Smith AH, Laird C, Porter K, Bloch M. Haemostatic dressings in prehospital care. Emerg Med J 2013;30:784-9.	This was an "educational review" "to summarise the literature on the main hemostatic agents that are currently available on the market for use in the prehospital environment."	Review of products on the market as of October 2012.
23	Zhang YJ, Gao B, Liu XW.	Zhang YJ, Gao B, Liu XW. Topical and effective hemostatic medicines in the battlefield. International journal of clinical and experimental medicine 2015;8:10-9.	Literature review mid 2014 crossing terms for hemorrhage, battle, wounds and injuries with hemostasis. Found 67 articles and kept 41 for review.	Limited review with no new information.

2019 Summary of Kept Articles for Review:

Authors	Full Citation	Year	Study Size	Agent Studied	Comments/Key Findings
Goolsby, C., L. Rojas, K. Moore, E. Kretz, E. Singletary, V. Klimczak and N. Charlton	Craig Goolsby, Luis Rojas, Krista Moore, Eric Kretz, Eunice Singletary, Victoria Klimczak & Nathan Charlton (2019) Layperson Ability and Willingness to Use Hemostatic Dressings: A Randomized, Controlled Trial, Prehospital Emergency Care, DOI: 10.1080/10903127.2019.1593566	2019	360 participants	S-fold vs Z-fold vs Plain Gauze vs Injectable gauze	Participants were **most successful with injectable gauze**. Study did not evaluate individual hemostatic gauze brands of products, rather it focused on the deployment method of the various types of gauze. Injectable gauze was the most successful.

Winstanley, M., J. E. Smith and C. Wright	Winstanley M, Smith JE, Wright C Catastrophic haemorrhage in military major trauma patients: a retrospective database analysis of haemostatic agents used on the battlefield Journal of the Royal Army Medical Corps Published Online First: 03 October 2018. doi: 10.1136/jramc-2018-001031	2018	317 patients	Hemocon vs Celox vs Quikclot against regular gauze	Retrospective review of casualties from the UK military trauma database. A **survival benefit was seen with the use of hemostatic dressings, when compared to non-hemostatic dressings**. Specifically, the authors concluded that a survival benefit was seen only in Celox. However, this could be a sampling error as, there was were significantly more cases of celox use (212) vs hemcon (87) vs quickclot (18).
Boulton, A. J., C. T. Lewis, D. N. Naumann and M. J. Midwinter	Boulton AJ, Lewis CT, Naumann DN, et al Prehospital haemostatic dressings for trauma: a systematic review Emergency Medicine Journal 2018;35:449-457.	2018	Systematic Review: 809 patients in the final analysis.	HemCon, Chitogauze, Celox Gauze, Quick Clot, Celox granules, Quickclot Granules, Quickclot ACS	712 titles were screened and ultimately 17 original studies were included. Limited to traumatic hemorrhage. Several questions asked including the clinical efficacy of hemostatic dressings for patients with trauma, which dressings have superior outcomes when compared to others. 8 civilian, 8 military and 1 combined study. Median reported **cessation of bleeding was 90.5%**. Most studies were rated as low or very low quality due to observational nature. Based upon data reviewed, the authors recommended combat gauze as the dressing of choice given how widely studied it is and it's safety profile.

Te Grotenhuis, R., P. M. van Grunsven, W. M. Heutz and E. C. Tan	R. Te Grotenhuis, P.M. van Grunsven, W.M. Heutz, E.C. Tan**Prehospital use of hemostatic dressings in emergency medical services in the Netherlands: a prospective study of 66 cases** Injury, 47 (2016), pp. 1007-1011	2016	66 patients	Hemcon Chitogauze	Retrospective review of EMS data from the Netherlands. Hemostatic gauze was used if conventional gauze did not work. Nontraumatic hemorrhage was excluded. Primary outcome was caseation of bleeding. 66 cases were included. **Chitogauze successfully stopped or slowed bleeding in 59 of 66 (89%) patients.** 21 of these patients had a clotting disorder and the hemostatic gauze was also effective in this population.
Leonard, J., J. Zietlow, D. Morris, K. Berns, S. Eyer, K. Martinson, D. Jenkins and S. Zietlow	Leonard J, Zietlow J, Morris D, et al. A multi-institutional study of hemostatic gauze and tourniquets in rural civilian trauma. J Trauma Acute Care Surg 2016;81:441-4. doi:10.1097/TA.0000000000001115	2016	40 patients	Combat Gauze	5 year Multi-institutional (10 sites) retrospective analysis of rural trauma cases of CG use and CAT TQ application. Primary outcome was cessation of bleeding. Protocol followed the ACS COT / NAEMSP protocol. 40 patients were treated with combat gauze which was reported to be **89% effective at cessation of bleeding**. Most often used on head/face (47.5%) followed by upper extremity (20%), lower extremity (15%) followed by other sites.
Zietlow, J. M., S. P. Zietlow, D. S. Morris, K. S. Berns and D. H. Jenkins	Zietlow JM, Zietlow SP, Morris DS, et al. Prehospital use of hemostatic bandages and tourniquets: translation from military experience to implementation in civilian trauma care. J Spec Oper Med 2015;15:48-53.	2015	52 patients	Combat Gauze	Retrospective review of patients with prehospital TQ and/or hemostatic gauze. Per protocol, hemostatic gauze was applied after conventional methods failed. A total of 62 dressings were applied to 52 patients with a **95% success** rate of stopping bleeding. The most common body locations were head/neck 50%, followed by extremity

					36%, followed by torso (5%) and junction (4%).
Travers, S., H. Lefort, E. Ramdani, S. Lemoine, D. Jost, M. Bignand and J. P. Tourtier	Travers S, Lefort H, Ramdani E, et al. Hemostatic dressings in civil prehospital practice: 30 uses of QuikClot Combat Gauze. Eur J Emerg Med 2016;23:391-4. doi:10.1097/MEJ.0000000000000318	2016	30 patients	Combat Gauze	Prospective observational study with Paris Fire Brigade. 30 cases of CG occurred. CG was used when conventional methods failed. **CG helped either completely stop or decease bleeding in 28/30 (93%)** of cases. No major side effects.

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3. National Research Council. 1966. Accidental Death and Disability: The Neglected Disease of Modern Society. Washington: National Academy of Sciences.
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5. McManus, J. 2007. Innovations in Hemorrhage Control. Presented at the International Trauma Life Support Congress, October 2007. San Antonio
6. King, K. 2004. Hemostatic dressings for the first responder: a review. Military Medicine. 169(9), 716-20
7. Wedmore, I et.al, 2006. A special report on the chitosan-based hemostatic dressing: experience in current combat operations. Journal of Trauma, 60(3), 655-58

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Additional Resources:

Anderson ID, Woodford M, de Dombal FT, Irving M. Retrospective study of 1000 deaths from injury in England and Wales. Br Med J (Clin Res Ed) 1988; 296:1305–1308

http://books.nap.edu/openbook.php?record_id=9978&page=1/ Journal of Trauma, 1971 Mar; 11(3): 195-206

HemCon home page:
http://www.hemcon.com/productstechnology/hemconbandageoverview.aspx

Jevon, P., Cooper, L. 2008. First aid. Part 5—First aid treatment for severe bleeding. Nurs Times. Jan 22-28; 104(3): 26-7

King, Kelly, 2004. Hemostatic Dressings for the first responder: A review. Military Medicine. 169, 9:716

Martinowitz, U. et.al 2004. Treating traumatic bleeding in a combat setting – possible role of recombinant activated factor VII. Military Medicine. 169(S1), 16-18(3)

National Highway Traffic Safety Administration. Trauma system agenda for the future. Annals of Emergency Medicine. 2003. June; 41(6): 798-9

Watters JM, Van PY, Hamilton GJ, Sambasivan C, Differding JA and Schreiber MA. Advanced hemostatic dressings are not superior to gauze for care under fire scenarios. *J Trauma* 2011;70(6):1413-9.

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